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# Pharmaceutical Executive

**JULY 2018**

COMMERCIAL INSIGHTS FOR THE C-SUITE

VOLUME 38, NUMBER 7



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# Blockchain 101 for Pharma Executives

**BLOCKCHAIN HAS BEEN DISCUSSED FOR A COUPLE OF YEARS NOW.** First, it's hype. Then it's a fad. Then, maybe, a glimmer of possibility. Then, it's "maybe we need one of those blockchain things." And depending on which area of the business you are working in, blockchain appears to have great potential to help certain aspects of drug development, specifically in the front end and back end—clinical trials and manufacturing. But having said that, blockchain is still in the potential but not proven area of the pharma enterprise.

I attended the Adverts Serialization Innovation Summit in Philadelphia last month, which had an impressive lineup of speakers around "Track and Trace" and the current US and EU regulations, as well as the industry compliance around that topic. Blockchain is but one way that serialization could be achieved. One of the experts from Microsoft offered a very thorough explanation around what blockchain is or isn't, and what executives should ask before going down the blockchain rabbit hole.

Tianna Umann, a solutions architect for Microsoft, explained that blockchain is not bitcoin. She called public blockchain "bitcoin 1.0." For professional or corporate purposes, enterprise blockchain would be the technology. It is not accessible by the public and doesn't represent a currency. For our purposes, from now on, blockchain refers to enterprise blockchain.

Umann also stressed what blockchain is NOT. It is not a data warehouse. It is not an internal database. It does not store data. It has no cryptocurrency. And it is not the solution to all of your problems.

So what is blockchain? Blockchain is single, trusted ledger by which all participants have a mirrored image and visibility to the ledger at the same time. The parties within the blockchain have to be admitted into the peer-to-peer system. And processes that are part of the blockchain are digitized and integrated into the blockchain.

No one can remove information or "delete" information in the blockchain. Any data in the ledger can be changed or over-written, but that is visible to all in the ledger in the peer-to-peer of who made what change, the time, and date.

When is blockchain the right choice for you? Umann suggested if any of the three following criteria fit your situation, then blockchain might be right for you.

- 1) Is it a process that crosses boundaries of trust?
- 2) Do multiple parties need to work on the same data?
- 3) Are there intermediaries that currently control the only source of truth? (these intermediaries may incur cost and decrease efficiencies.)
- 4) Does the process involve manual verification steps that have low value?

[Blockchain] is not a data warehouse. It's not an internal database. It does not store data. It has no cryptocurrency. And it's not the solution to all of your problems.

Umann continued that some of these questions could be a database fix, and not necessarily in a blockchain deployment. Additionally, there are current concerns that blockchain may be slow. A current popular public blockchain, Ethereum, is not proving to be scalable with low data per second transfer speeds. Umann said that each system has to validate identity, logic, and properties, which takes time and is based on the computing power of the peer-to-peer distributed systems.

Many in the audience believed with Umann that there are clear use cases for blockchain, including DNA sequencing, health data, prescription data, and personalized medicine. Use cases should start appearing soon, so we will wait for theory to practice.



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# Pharmaceutical Executive

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# Compliance: Critical Cog in Pharma Machine

Lisa Henderson, Editor-in-Chief

Getting ahead of legal and compliance issues in the life sciences requires a lot more these days. *Pharm Exec* convenes an expert panel at CBI's Pharmaceutical Compliance Congress to discuss new ways to navigate the many complexities when it comes to the crucial task of assessing business and risk.

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On the cover (clockwise): Patrik Florencio, of Amicus Therapeutics; Michael Shaw, of GSK; Seth Lundy, of King & Spalding; Ellen Rosenberg, of Amicus; Tom Gregory, of Ernst & Young; and Evan Bartell, of KPMG.

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### Correction

In the article, "2018 Pharm Exec 50," published in the June 2018 issue of *Pharmaceutical Executive*, some of the companies ranked in the included tables are incorrectly ordered. For updated and corrected Top 50 rankings, please visit here: [bit.ly/2yOuPSQ](http://bit.ly/2yOuPSQ)

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## Top Stories Online

**2018 Pharm Exec 50**

June issue online  
Michael Christel  
[bit.ly/2yOuPSQ](https://bit.ly/2yOuPSQ)

**Top 10 Industry Trends to Watch**

Blog post  
Archbow Consulting  
[bit.ly/2APV9rt](https://bit.ly/2APV9rt)

**2017 Emerging Pharma Leaders**

October issue online  
Pharm Exec staff  
[bit.ly/2ij0qRo](https://bit.ly/2ij0qRo)

**Pharma Reputation Rankings Unveiled**

News post  
Pharm Exec Staff  
[bit.ly/2t0hjGJ](https://bit.ly/2t0hjGJ)

**Digital Health: It's Not All About the App**

Blog post  
Julian Upton  
[bit.ly/2yUiLQc](https://bit.ly/2yUiLQc)

Most-read stories online:  
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## Pharm Exec Webcasts

**A Framework for Successful Biopharma Product Launches**

[bit.ly/2yR1Tts](https://bit.ly/2yR1Tts)

*On-Demand***Evolving Life Sciences Quality Management**

[bit.ly/2N9dpUr](https://bit.ly/2N9dpUr)

**Combination Therapies & Oncology Landscape**

[bit.ly/2JcY3Pf](https://bit.ly/2JcY3Pf)

**Patient Engagement in Clinical Trials**

[bit.ly/2FjjZSW](https://bit.ly/2FjjZSW)



## Readers Weigh In

There is a way to give the pharmaceutical industry a means to lower drug prices. Increase the years of patent for brand-named drugs. Make a deal with the brand-name development companies to give them time to gain back the \$\$\$ they put into research to bring their drugs to market. Lower the brand drug price and gain the profit over time, instead of them rushing to gain back their expenses in the short time they have to market their drug before the generic companies take over the market.

Anonymous

"Can Trump Plan Serve as Model for What Ails Europe?"  
[bit.ly/2IH8nlv](https://bit.ly/2IH8nlv)

What you say is very true. I've just finished my PhD on medicine adherence. There's a huge amount that manufacturers/distributors could do to improve adherence in many different areas concerning the product—supply chain, patient skills, etc. It's an area crying out for some focus, but, sadly, my experience mirrors yours.

Anonymous

"Adherence: Addressing Pharma's Last-Mile Problem"  
[bit.ly/2tM0Wgw](https://bit.ly/2tM0Wgw)

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industry leaders, as well as providing a behind-the-scenes look at what the editors at *Pharm Exec* are working on.

The *Pharm Exec* Podcasts are available on all your favorite listening tools such as iTunes, SoundCloud, Google Play, Stitcher, and Overcast. Here's a peek at our recent podcasts, with links to listen!

#### Episode 11: Tackling Sports and Science

Former NFL star and current broadcaster, Solomon Wilcots, talks to *Pharm Exec* about the intersection of sports and biopharma, including his work in matching pro athletes who are passionate about a certain disease with biopharma organizations. [bit.ly/2YRP6HV](http://bit.ly/2YRP6HV)

#### Episode 10: Mentorship vs. Sponsorship

Michelle and Christen host one of *Pharm Exec*'s Emerging Pharma Leaders, Sabina Ewing, vice president of business technology for Pfizer, who discusses the difference and importance of mentoring and

sponsoring in business and pharma. [bit.ly/2IAoiLf](http://bit.ly/2IAoiLf)

#### Episode 9: Brands of the Year

Michelle and Christen host the *Pharm Exec* editorial team to discuss our selections of Brands of the Year and why we chose to highlight these particular products. [bit.ly/2ILwFZe](http://bit.ly/2ILwFZe)

#### Episode 8: CFO in Focus

Tim Sullivan, chief financial officer of Apellis Pharmaceuticals, provides an inside look at what it takes to be the CFO of a development-stage biotech company, and what business skills are needed to succeed in that type of position. [bit.ly/2Ilfwig](http://bit.ly/2Ilfwig)

#### Episode 7: Big-Event Insights

*Pharm Exec* editors discuss key takeaways from a variety of industry conferences that took place across the globe. [bit.ly/2Fhfto4](http://bit.ly/2Fhfto4)



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# Regulatory Innovation Generates Breakthroughs

Streamlined clinical research, more guidance speed new cures to patients

**F**DA is overhauling its new drug review process and launching new pilots and strategies to modernize clinical research and data analysis in order to move more cutting-edge therapies through the regulatory process to patients. Reports of positive outcomes and extended benefits from targeted cancer treatments at the June meeting of the American Society of Clinical Oncology (ASCO) generated great enthusiasm for genetic analysis and immune marker testing to better match treatment to disease markers in the growing field of precision medicine. New incentives, moreover, promise to encourage the development of much-needed antibiotics, and gene and cellular therapies are emerging from initiatives to streamline testing and oversight of innovative biologics.

While biopharma companies and the research community applaud these efforts, skeptics continue to raise concerns that long-term safety risks, unsure efficacy, and high price tags may limit benefits and keep important treatments out of reach for many individuals (see sidebar on facing page). FDA Commissioner Scott Gottlieb maintains that less costly clinical research and faster approvals should boost competition in pharmaceutical markets and bring down the cost of

many important drugs in the process.

## More efficient studies

At the ASCO meeting, Gottlieb outlined FDA efforts to keep pace with medical innovation through updates in clinical trial operations, regulatory policies, and manufacturing standards to create a more efficient, less costly and more innovative review process (see <https://bit.ly/2ym4b3O>). For example, FDA is testing a program that permits reviewers to assess a sponsor's clinical trial data before the application is filed to ensure that submissions contain all relevant information needed for a timely review. Another strategy involves creating a common review template for both FDA staffers and applicants to record comments and answer questions, avoiding multiple parallel review documents.

There's also great excitement over the emergence of new cellular and gene therapies, with three innovative products on the market and analysts reporting more than 500 in early development. FDA's Center for Biologics Evaluation and Research (CBER) has established policies and procedures for overseeing treatments that qualify for the Regenerative Medicine Advanced Therapy (RMAT) designation, and CBER plans to issue further guidance documents to clarify manufacturing and testing

policies, starting with hemophilia treatments. Because these therapies target devastating diseases, FDA expects to approve promising products based on surrogate measures, with post-market studies using registries and real-world patient evidence to document continued benefit or safety issues. CBER also seeks to clarify ways to deal with the complex production and scale-up issues for these biotech therapies that often delay product approval and marketing.

While scientists are pursuing extensive research to treat cancer and genetic diseases, efforts to combat the spread of drug-resistant infections have been limited, as R&D difficulties and financial impediments have discouraged development of innovative antibiotics and antimicrobials. A new research strategy may help, as seen in recent FDA guidance on how manufacturers may utilize streamlined research methods and accelerated approval policies for therapies that qualify for the Limited Population Pathway for Antibacterial and Antifungal Drugs (LPAD).

To spur industry investment in this field, Gottlieb recently proposed a licensing model with a "pull incentive" to ensure manufacturer reimbursement for new infectious disease treatments. The idea is that hospitals and clinics would pay a fixed licensing fee to access a certain volume of doses of the new medicine, creating predictable revenue for the developer, while discouraging excessive use of the new treatment that often leads to resistance.

## Getting personal

These R&D initiatives aim to further tap patient expertise on evaluating burden of disease and treatment preferences in design-



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ing research strategies. FDA has moved over the last decade to achieve a more systematic approach for incorporating patients' experiences into the clinical testing process and continues to seek better ways for measuring and collecting patient experience data, such as registries to identify in advance those patients who meet enrollment criteria. Initiatives to advance precision oncology treatments involve assessing patient-reported outcomes (PROs) in cancer trials and FDA use of PRO data in regulatory review.


The agency recently published the first of several guidances that aim to further utilize patients' perspectives in drug development. This draft advisory recommends methods for collecting patient data in clinical trials (see <https://bit.ly/2sY1Jez>), and additional guidances will provide more specifics on using interviews and survey informa-

tion, on identifying issues most important to patients, and in selecting patient-focused study endpoints. The overall goal is to map out sound methodology for collecting patient input so it provides valid data that can inform regulatory decisions.

Maintaining a speedy, efficient new drug review process is vital to FDA's success in encouraging innovation and speeding new breakthrough therapies to patients. To be able to assess the growing volume of promising new drugs and biologics in accelerated and compressed timeframes, the Center for Drug Evaluation and Research (CDER) is overhauling its Office of New Drugs (OND).

Janet Woodcock, CDER director, has led the reorganization initiative this past year, with an eye on encouraging team-based reviews and systems to make the oversight process more efficient and consistent. A "flatter" OND will have

## Gottlieb recently proposed a licensing model with a "pull incentive" to ensure manufacturer reimbursement for new infectious disease treatments

nine instead of five drug review offices, with up to 30 specific review divisions. CDER staff must deal with a "staggering pace of work," Woodcock said, and that involves attention to detail and keeping up with emerging scientific advances in genomic medicine, targeted therapy, digital health, drug-device combinations, and more global drug development programs. 

### Speed vs. safety?

In addressing the ASCO meeting in June, FDA Commissioner Scott Gottlieb described how FDA was advancing the science of drug development and moving away from "anachronistic" clinical trial constructs, "where failure is typically expensive and routine, and success is the exception." With such a large number of new cancer drugs in development, he said, "there literally is not enough time, capital, or patients to test these approaches conventionally."

To FDA critics who regard such changes in regulatory policy as forcing a choice between speed and safety, Gottlieb countered that regulatory decisions are not "a zero-sum game." FDA seeks modern and efficient policies to ensure that drug development is less costly, less risky, and less time consuming to enable more patients to benefit sooner from new advances. Cancer patients, he observed, don't want to wait three more years for another large, prospective, randomized trial to be completed to prove overall survival.

Not all experts agree, as articulated in a lengthy *New York Times* editorial in June that describes FDA's efforts to speed new drugs to market as "lowering the standards" for deciding whether a new medication is safe and effective. The commentary wants to limit approval to those therapies that demonstrate long-term benefits, such as prolonging life, in at least two clinical trials (see <https://nyti.ms/2M3THb2>).

FDA experts acknowledge that more streamlined development programs should carry post-market surveillance requirements to assess continued benefits of new discoveries. At the same time, health plan coverage policies should provide patient access to potentially life-saving medicines. Targeted cancer drugs and gene therapies will never be cheap and easy to test and produce, and society needs to manage the high cost of developing these cures for those few individuals likely to experience important benefits.

# The Rise of China Biopharma

Exploring the prospects—and related challenges—for Chinese life science as it aggressively pursues new growth areas

**T**here has been a great deal of interest in China on the biopharmaceutical and healthcare fronts for quite a while and that interest continues to escalate. If you go back in history, it was not long ago that China was principally a low cost, low quality producer of pharmaceutical intermediates and fine chemicals, along with many companies from India. Subsequently, there was a forced clean-up of manufacturing practices that significantly improved the reputation of Chinese-sourced active pharmaceutical ingredients (APIs) and fine chemicals. The Chinese pharma firms were also producers of traditional Chinese drugs and many generic pharmaceuticals for local and international consumption.

Since then, the Chinese have moved up to be more global producers of generic drugs and are beginning to manufacture and even develop more sophisticated medicines, some of which are proprietary to the Chinese biotech or pharma companies. There are even increasing numbers of Chinese biotech and pharma organizations that are conducting clinical trials for drug candidates in China and the US simultaneously.

On the regulatory front, it has been a bumpy road for the Chinese FDA as it struggled to develop and implement standards and approval procedures that were appropriate for the Chinese market and increasingly in line with the US FDA and the European Medicines Agency (EMA). There is increasing respect for the Chinese regulatory system now in

China and abroad. Also, as is the case for the US FDA, the Chinese FDA is trying to streamline its approval process without compromising science and public safety.

In terms of the Chinese healthcare market, the attraction of a very large population has always drawn a great deal of interest on the part of both Chinese and Western providers of drugs. China has gone from a system with no healthcare insurance and a hospital-centric healthcare system to the introduction of healthcare insurance and a more diversified, modern system of providing patient care.

Lastly, the Chinese are trying to create the very delicate ecosystem that exists in selected parts of the world that is required to attract leading researchers, develop drugs successfully, establish and fund biotech companies, and provide the providers of capital with the liquidity and valuation increases that are critical to the success of biopharmas in the West.

The history of new drug development ecosystems in various cities and countries around the world has had a very mixed record of failures and successes. The number of regions that have tried and failed is significant. Those that have studied this phenomenon believe that there is a delicate balance of strong research universities; government-sponsored research organizations (such as NIH and DARPA in the US); pharma companies with the right mix of tools and people; funding sources at every stage of product development of a biotech; a regional stock

market that will support emerging biotechs; and the right living environment that can attract the best researchers.

China has been working very hard to try to create successful biotech/drug development ecosystems in various locations in China. These efforts include massive funding focused on graduating large numbers of university-trained Chinese scientists, encouraging the growth of venture capital and private equity funds that can invest in Chinese biotech/pharma, and the recent designation of biotech as one of the targeted industries that Chinese wants to achieve an independent major position in by 2025. Other targeted industries include robotics, aircraft, and electric cars.

In addition, the Chinese government changed the rules with regard to IPOs in Hong Kong that allow biotech and technology companies that do not have revenues to go public, subject to certain rules and restrictions, on the Hong Kong exchange. Previously, companies without revenues could not go public in China on any of the exchanges, and the only option for Chinese biotechs to go public was in the US or Europe via an IPO or reverse merger. It is not yet clear how many Chinese biotechs will go public on the Hong Kong exchange, but there is no question that the public market valuations in China across many industries are substantially higher than those in the West. Whether this is sustainable or not is not clear. However, for the moment, it does give Chinese companies that are public a clear advantage in terms of their cost of equity.

It is not yet certain whether the Chinese government and pharma/biotech community will achieve the targeted goal by 2025 or, more importantly, whether it will be



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able to create successful and stable ecosystems. It is clear that the Chinese are very intent on trying.

**Opportunities**

The list of opportunities for both Chinese and Western pharma and biotech companies is substantial. To start, the Chinese market for drugs is mushrooming and the incentives to sell existing and new drugs into the Chinese market are high. Although there are pricing, intellectual property, distribution, and regulatory issues to deal with, the overall opportunity is positive, but very much driven by the specifics of each drug and company.

In addition, with many now established Chinese biopharma companies, Western drugmakers

are regularly partnering or licensing product candidates or US-approved treatments with Chinese organizations. The other opportunity is that there are an increasing number of new drugs that are being developed by Chinese companies where the clinical trials and marketing in the US or Europe will be better handled by a Western biopharma company with regional regulatory expertise, in-place sales and marketing resources, and, if needed, funding.

Lastly, although the revision of the Hong Kong Stock Exchange IPO rules will primarily benefit Chinese biotech IPOs, it will also be open for dual listings by Western biotechs, which could enable access to more Chinese investors.

**Threats**

There are also threats, although the list is not as long as the opportunities. The obvious threat is the potential for Chinese biopharma companies to eventually become aggressive competitors in the more attractive therapeutic areas, aided by government support; looser standards around issues such as the use of genetic engineering; easier availability of private and public equity funding at higher valuations; and the dramatic increase in university research and graduates.

Whether the Chinese can gain significant share over time in the market for more sophisticated drugs is still an open question, but it's clear that its government wants the industry to achieve that goal. **PE**

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# Compliance: The Critical Cog in Pharma Machine

Getting ahead of legal and compliance issues requires more these days. At CBI's Pharmaceutical Compliance Congress, experts gathered to discuss new ways to navigate the many currents in the industry when it comes to the crucial task of assessing business and risk

## Roundtable Participants

**Evan Bartell**, Advisory Managing Director, KPMG

**Patrik Florencio**, Senior Vice President, Chief Compliance and Risk Officer, Amicus Therapeutics\*

**Tom Gregory**, Partner, Fraud Investigation and Dispute Services, Ernst & Young

**Seth H. Lundy**, Partner, King & Spalding LLP

**Ellen Rosenberg**, Global General Counsel and Corporate Secretary, Amicus Therapeutics\*

**Michael Shaw**, Vice President, Ethics and Compliance Officer, US Pharma, GlaxoSmithKline

**Lisa Henderson** [moderator], Editorial Director, *Pharmaceutical Executive*

*\*interviews conducted after the CBI roundtable and edited in*

**L**ike most instances in corporate compliance, hindsight is 20/20. Unfortunately, for the biopharma industry, any number of negative compliance issues can cause political, legal, public image, and reputation problems that potentially could take a number of years from which to recover.

However, pharmaceutical compliance covers such a broad spectrum of potential problems, from day-to-day HR compliance, to foreign corruption and bribery, patient assistance programs, drug pricing and transparency, off-label communication, manufacturing, opioid and Department of Justice (DOJ) issues, and so much more. Changing regulations and laws, as well as potential business practices that aren't yet deemed illegal, keep com-

pliance executives and pharma counsel on their toes.

Recently, the DOJ has placed attention on the practice of pharma companies donating money to charitable patient assistance programs, specifically those that help patients defray drug co-pays or total drug costs. Regulators have noted that when such donations aren't managed in an appropriate way, they can raise concerns under the Anti-Kick-back Statute. Recent settlements between pharma companies and the DOJ were discussed and analyzed in sessions at CBI's Pharmaceutical Compliance Congress (PCC) to help others navigate these new waters.

At PCC 2018, held at the end of April in Washington, DC, *Pharmaceutical Executive*, with our meetings partner CBI, held a roundtable discussion to assess the state of the compliance role within the biopharma industry.

**PE:** *In your experience, how does compliance get a seat at the table? Do they have a seat at the table? Or is it a mix?*

**MICHAEL SHAW, GlaxoSmithKline:** You have to earn it by value. We know that our business leaders will resource what they value. We need to understand the environment, the associated risk, and, more importantly, apply it to the business practices in a relevant way so that we can enable the business to be competitive and compliant. When you do that, business will want compliance at the table.

**TOM GREGORY, Ernst & Young:** With the clients that I work with, it's very varied. By and large, at multinational companies, compliance is very mature, sophisticated, and has access to executive management, which is



(Left-right) Seth Lundy, of King & Spalding; Michael Shaw, of GlaxoSmithKline; Tom Gregory, of Ernst & Young; and Evan Bartell, of KPMG, pose at CBI's PCC 2018 in Washington. Not pictured, but incorporated into the roundtable discussion, were Patrik Florencio and Ellen Rosenberg of Amicus Therapeutics. Both were presenters at the event.

clearly adding value. Where I see gaps is in the less-mature companies—the start-up space or certain non-US markets—where compliance hasn't received the attention and the resources that it has in the United States.

**SETH H. LUNDY, King & Spalding:** What we mean when we say access to a seat at big tables is access to the board and executive teams on major decision-making within the corporate realm. The challenge that compliance as a function continues to have is the staffing abilities of compliance or legal departments, which means they can't have a seat at all of the tables that are ongoing simultaneously within a company.

But having said that, sometimes you see start-up companies, when the compliance officer is the 15th employee at the company, and 15 people are always sitting around the table,

you're getting compliance input at every germinating thought and seed.

But what if you have a 5,000-person commercial force and 40 compliance personnel to oversee them? There are meetings and ideas that are coming up all the time where compliance isn't a part or invited or being asked the questions. And compliance can only address questions that are effectively asked or that are within its visibility. So, oftentimes you only see that through later auditing and monitoring.

**SHAW:** Seth, I somewhat agree. But I think we've got to be careful because compliance should not need to have a seat at every table or at every discussion. If we want compliance to be sustainable in an organization or an industry sector, then ultimately the business has to own compliance. And, just like a

“This industry has become so incredibly complex, that even within your compliance departments you must have different experts to address different areas.”

— SETH LUNDY, KING & SPALDING



CEO looks to their leadership team to deliver certain performance objectives during a year, they should hold their management team accountable to also know ahead of time what the big risks are and what they're going to do to mitigate them.

**LUNDY:** The fact of the matter is this industry has become so incredibly complex, that even within your compliance departments you must have different experts to address different areas, because one person can't possibly be able to retain all of the information. Therefore, in any given business meeting, expecting that the business is going to have information that even trained compliance personnel don't have in every instance is a challenge unto itself. Some companies use liaisons who are not in the compliance department but are more specifically trained through compliance, and delegating them responsibility, is in and of itself a compliance function.

**PE:** *We just touched on the resource issue for smaller companies as a benefit and a challenge. What is your experience in regard to the smaller biopharma?*

**EVAN BARTELL, KPMG:** In large and small organizations, it's really about the relationships. In a

small company, with a single compliance officer or a compliance team of maybe two or three, they can enhance their effectiveness when the right relationships are created with the right people within the business. So, it's not, “Hey, just tell me everything that's happening”; but it's, “Hey, you understand what my goals and objectives are, I understand what your goals and objectives are, let's help each other.”

**ELLEN ROSENBERG, Amicus Therapeutics:** You need collaborations with finance, legal, regulatory, HR, QA, and others that have compliance responsibilities in any company, but it is especially important if you are in a smaller company, with more limited resources; you can rely on strong collaborations to achieve compliance objectives.

**PATRIK FLORENCIO, Amicus:** Well-trained business executives who are committed to compliance become an extension of compliance and legal and the values these functions represent. I've worked with many business partners over the years who have become extremely knowledgeable about compliance risk and who think about compliance when they are rolling out innovative new ideas. To some, it comes naturally. To others, less

so. But the key is to spend a lot of time having conversations, explaining the “why,” so business partners can self-identify issues and bring them to us. That creates awareness within the business, the function that's conducting the activities.

**PE:** *Is an ethical and compliant company built up with good people that you hire? Is it an attitude? Or is it from the top down?*

**SHAW:** Management needs to drive it. That's the differentiator in so many decades hearing about tone at the top or tone at the middle. Management needs to drive, because most good leaders know “you get what you inspect.” If their message is all the time, “Perform, perform, perform and, oh, by the way, comply,” then you should not expect to get a culture like you would if the message was, “We're going to do this the right way and make sure we effectively navigate the risks that will challenge business performance and our organization's mission and values.”

**LUNDY:** The tone that we're talking about is set in three different ways. When we talk about tone at the top, that means not just verbal messaging, but also action and budget. And you have to have all three of those things happening simultaneously for the tone to be most effective.

**FLORENCIO:** It is helpful when a company's leadership believes in an overarching concept of performance with high integrity. Nobody wants to work at or for a company that doesn't perform. Everybody wants to be with a successful company. But to do it with high integrity can sometimes be challenging because everyone comes at it from differ-

ent perspectives or different levels of risk tolerance.

On an individual level, risk tolerance is greatly impacted by the past personal experiences of the people you are dealing with. The people who have been deposed or have gone through a formal investigation see compliance in a very different light. They are much more open to hearing the advice of the compliance officer and legal because they don't want to go through it again. And they are much more willing to work with you to achieve the objectives they want to achieve. The goal is never to just say no, but to take a different route or take the same route with different controls to make it safe.

**ROSENBERG:** There is an element of who you hire in the key roles in your company. Compliance and legal should be involved in the interview process for those who are going to be in potential key stakeholder positions so that people who are like-minded are hired. People who are committed to business ethics. If you don't want a mixed bag and are looking to build a culture of integrity, then you have to have that in who you hire, and you have to have that in who you involve in the hiring process. I think that's an important element in building a compliance-minded culture.

**PE:** *How do you stay on top of, or ahead of potential problems? For example, the issues coming up with patient assistance programs. How could compliance mitigate that before it becomes a problem?*

**GREGORY:** It's a question of not fighting yesterday's battles. If you're just doing what a CIA\* requires, you're maybe only



“If you are looking to build a culture of integrity, then you have to have [a commitment to business ethics] in who you hire and who you involve in the hiring process. That's an important element in building a compliance-minded culture.”

— ELLEN ROSENBERG, AMICUS

chasing the bad conduct of a decade or two decades ago. How do you spot things that are going to be the subject of enforcement actions in the future but maybe have not been in the past?

With patient assistance, did anybody see that coming? I think that's debatable. But there are probably five to 10 other similar practices where there's not historically been enforcement action, but the government will at some point turn to that and start suggesting that the practice is violative of some law or regulation.

**LUNDY:** When we talk about things like patient assistance as a growing area of risk, it is easy to have some level of compliance ignorance. As a defense attorney, every case that I handle is involving conduct that happened a minimum of three years ago and oftentimes eight to 10 years ago. If you're looking for only—as Tom was indicating—those things that someone has already demonstrated that this was the wrong path, you're looking back at things that people did five to seven to 10 years ago. And that's not novel or instructive of where the risk is today and what some-

one's going to be looking at five years from now.

**FLORENCIO:** Looking to the future, I think businesses should partner closely with compliance and legal in building out their patient engagement programs. This is such an important area and one that is poised to deliver increasing value back to patients and communities as time goes on. That said, because patient advocacy departments are growing and engaging in new and innovative activities at every phase of a medicine's lifecycle, these activities must be thoughtfully structured so as to deliver value to patients without sacrificing compliance.

We already know that patient-related activities are a focus of DOJ enforcement, albeit on the hub side for now. But enforcement could expand to other areas like patient field interactions in the future. We know, for example, that HCP (healthcare professional) field interactions has been a huge area of enforcement for years. So, when you put it all together—increased patient interactions, including in the field, at a time when DOJ is already focused on patient-related

“Management needs to drive [compliance], because most good leaders know ‘you get what you inspect.’”

— MICHAEL SHAW, GLAXOSMITHKLINE



activities—we know this is an area where we should be careful. The compliance function should be thinking about patient field activities and helping the business to appropriately structure those interactions while still serving the overarching goal of patient centricity.

**ROSENBERG:** You also have to have some common sense about this. If you understand that the government in the past has been focused on following the money, for example, the focus on HCPs, and if you follow the money and you are putting a lot of money into patient-related activities, whether it's foundations, hubs, patient support services, or other interactions, then you need to look at those things to predict where the enforcement has been in the past. I just think you need to be practical and smart to get the right kinds of controls in place and the right visibility in place for these activities.

**BARTELL:** It's also being plugged into the business and knowing what their challenges are, particularly within patient access. There's a lot going on now in the industry in terms of how patient access works, how co-pay programs are going to work or look in the future. The more that compliance professionals understand the challenges that the commercial and business folks are facing coming up

with solutions to potential barriers and problems that their brands are going to be facing, the more successful compliance will be. Because if you understand that fundamental challenge that your business is facing, then you can help them navigate from a risk management standpoint.

**LUNDY:** You also need to be plugged in with the various communities, by coming to congresses like PCC, to be able to identify what's going on with peers, what other professionals are seeing in the marketplace, or interacting with panels like we had with prosecutors to hear what's on their mind. You need to have an outside resource that you can check in with. The value of consultants, attorneys, and peers are to see what else is going on in the industry that you wouldn't know about just by being back at home.

**PE:** *What about the nuances of third-party involvement? Some programs evolve very quickly, and how does that get managed?*

**GREGORY:** The framework is basically four pillars: 1) conducting due diligence on your third parties; 2) contractual protections making clear what their obligations and responsibilities are; 3) audit rights that you exercise to monitor what they're doing; and 4) back-end monitoring or analysis of data

and such to oversee what they're doing.

**LUNDY:** I would use the fourth as a way to help to ensure that there is an ability to cut bait or terminate—walk away, when necessary. And that goes back to setting the tone of compliance. If you don't come back and audit, if you're never willing to terminate an independent contractor arrangement, then it sends a message or tone throughout the company, and other suppliers as well.

**BARTELL:** I do think in terms of the patient-support programs—your hubs, reimbursement services, co-pay vendors—that a trend is historically these programs were built out in silos, within certain therapeutic areas and franchises. These teams would go to their preferred vendors and manage the programs their way. I think the industry has taken a step back and looked at that to say that system needs to be more efficient and consistent. We need to consolidate. There's a movement to bring things together and consolidate across departments and functions, especially in large organizations.

**FLORENCIO:** Two keys are visibility and partnership. Visibility comes when business functions develop strategic plans and share those plans with compliance and legal. Just like marketing develops marketing plans, advocacy can develop a yearly patient engagement plan and share it with compliance and legal. The same is true for medical. This allows innovative ideas to be discussed at the conceptual stage, and any compliance considerations to be woven in, before they are implemented in the real world. The yearly



strategic plan is only the first step to visibility and partnership. As strategies evolve throughout the year and as new ideas arise, these should be shared with compliance and legal through a process of ongoing concept reviews. That's good partnering.

**PE:** *How do you review or reinforce compliance throughout the company?*

**SHAW:** Compliance should be more than just straight compliance with the law. Each organization should have a meaningful risk management approach. And that means taking a moment out of time and thinking about what those risks are based on the environment, based on the practices of any one company, and then asking, "How well are we doing here?"

Part of that answer comes with checking out what the most recent guidance has been, what the most recent investigations have been, and what the most recent practices have been.

**LUNDY:** It's the continuous part of the process that has to happen. If you do something once, that's great; but if you haven't done it in some regular period of time thereafter, the world continues to change and it can pass the corporation by. There isn't a prescribed period, but there ought to be some regular process that occurs so that you're constantly doing a checkup.

**SHAW:** And the continuous process is not only just adding on or being more conservative. It's revisiting processes and finding undue complexity, where we thought the way to manage a few years ago on a particular topic was one way and we realize it's totally hampering the



"As chief compliance officers grow to view themselves more as chief risk officers who look past the current enforcement landscape

toward what is likely to be enforced next, we may become a more proactive profession."

— PATRIK FLORENCIO, AMICUS

business and may not even be mitigating the risk we thought it was in the first place.

I have a fond memory working with you, Tom, at one point, when EY was our independent review organization. Even we had very positive results; at times when you would share with me minor deviations of a process, you looked at us and said, "Listen, your process has 10 steps to it. The process only needs two or three steps to address the risk. But if you have the 10 steps and you miss one of them, we're going to cite you for a deviation."

**LUNDY:** I think companies get inappropriately faulted, though, too, because awareness doesn't necessarily mean that the issue has been fixed or addressed. When you become aware of a risk, there's an entire process that necessarily needs to take place to be able to understand, address, and mitigate that risk. And that process takes time, particularly when the risks are new. Even when compliance is working 100 percent as it should, you can't necessarily snap your fingers and immediately mitigate risks as soon as they're identi-

fied. That's an unfair expectation to put on corporations and certainly compliance departments.

**FLORENCIO:** As chief compliance officers grow to view themselves more as chief risk officers who look past the current enforcement landscape toward what is likely to be enforced next, we may become a more proactive profession. But even so, it's hard for compliance officers to convince their business not to do something or even to do it in a different way when three factors are present. Competitors are doing it. There is no existing enforcement to point to. And the only argument to adopt a different practice is the compliance officer's prediction of future enforcement. If those three things are present, even today, it's difficult to win the day unless you have a very strong culture of compliance. <sup>PL</sup>

\* The Corporate Integrity Agreement, or CIA, is an enforcement tool of the US Department of Health and Human Services' (HHS) Office of the Inspector General (OIG) and is part of a settlement agreement arising from allegations of healthcare fraud.

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## Patient- & Customer-Centric Commercialization: A Case Study

Outlining a real-world example in which building and operationalizing a patient- and customer-centric commercialization strategy drove a successful launch from a “standing start”

*By Wills Hughes-Wilson, Alan Raffensperger, and Birgitte Volck*

**P**atient-centricity and customer-centricity are high on the agenda of many pharmaceutical companies. Most state that they are patient- and customer-centric or have an aspiration to be so. But what does that look like in reality, and how does one create, build, and lead a patient- and customer-centric approach from an operational perspective? And is it merely a branding or “feel-good” exercise, or can this approach drive deeper benefits, both from a business perspective and in terms of employee engagement?

Such an approach can actually drive both, which may be a critical differentiator when “time to launch” and return on investment is under increasing pressure, and at a time when engaging effectively with the workforce to bring best results

with tightened resources is a defining success factor for leadership teams.

### Doing the right thing, the right way

Many decision-makers are critical to the successful launch and commercialization of a new treatment. Regulatory authorities must approve a new drug; physicians have to believe in the utility of the product and understand where it fits in their therapeutic arsenal; payers or reimbursement authorities need to agree to fund it; and, ultimately, patients and their families have to believe that they will benefit from it.

This means there is a complex series of stakeholders and decision-makers—essentially customer communities—that needs to be engaged to deliver the successful launch and commercialization of a new drug. And when different effective treat-

ment regimens are established, finding a place for a new drug can be a challenging and complex process, particularly in some rare disease areas, where communities can be close-knit.

In order to meet these challenges, the leadership team, in this case study, identified “Patient- & Customer-Centric Commercialization” as a way of operating. The objective was to create an organization that actively sought dialogue with each decision-maker or stakeholder to understand their needs, and to create collaborative approaches to respond to those needs; in other words, a unified cross-functional launch team—commercial, medical affairs, and access—supported by HQ functions, whose operating model was based on listening and responding, rather than “talking and telling” or selling.

Each function within the launch team consulted as early as possible with the decision-maker, or customer, at each stage of the process to bring their concerns or needs into the internal strategies and decision-making; the resulting plans and roll-out were built on the basis of addressing these concerns. This started with building a total understanding of the patient journey—the experience and the touchpoints that a person with a given condition experiences. This set of experiences and interactions served as a roadmap for the launch teams. By understanding this and then treating each decision-maker as a facilitator rather than a barrier, seeking to align the company’s approach to the decision-makers’ insights at each step in the development and availability process, the teams were able to create integrated and impactful out-

comes. Indeed, all country launch plans were required to include a fully integrated commercial, medical, and access approach with an accompanying map of the respective “patient journey” for that country. This map included the stakeholder and support network, with actions for how to appropriately support and engage.

## The result of this approach was a launch franchise getting to market in shorter timelines than the industry average in almost every European country

The result of this approach was a launch franchise getting to market in shorter timelines than the industry average in almost every European country, reaching almost €300 million in European revenues in just two years. The company went from being a relative unknown in a competitive field dominated by big pharma companies in 2012 to top rankings in the therapeutic area by 2017 and trusted as a brand. The company was also able to negotiate price increases for a product that was, for historical reasons, dramatically underpriced to the level of commercial unviability in some key markets. Rather than being forced to withdraw the product, the company was able to work with health authorities to secure more realistic prices that allowed it to continue to make the treatment available.

The approach also had a motivational effect on the internal company community, creating a workforce that felt genuinely engaged and empowered to deliver. Aligning alongside the patient journey to understand what customers at all stages of

the process wanted and needed and creating a built-in approach that aligned with those needs were aspects that harnessed employee motivation. At a time when resources are stretched, inter-generational interactions between leaders and incoming talent is a key focus; the ability to engage across the organization is a core leadership skill. A

cross-functional, cross-border focus on the patient was a key element in creating motivation and a sense of purpose.

The approach to building and operationalizing a patient- and customer-centric business took place against a backdrop where interactions with all stakeholders are under the spotlight and stakeholders themselves are alert to perceived undue influence. In many parts of the decision chain, interactions are strictly regulated—there are clear rules about when and how companies may communicate with regulatory authorities, and how company-physician or key opinion leader (KOL) interactions should happen. Other stakeholders, such as patient representatives, are guided by codes of conduct. Thus, what is appropriate outreach or interaction is in the hands of the company and its individuals. The way *not* to do it may only be discovered after mistakes have been made and the repercussions felt by the organization and the business.

It was vital to orient all members of the company around the rapidly changing external envi-

ronment and appropriate behaviors, taking into account not only the legislative framework, but also individual accountability. In a diverse business with many different conversations happening across geographies, business units, and functions, reliance on heavy rules can lead to inertia; individuals can become fearful of taking the initiative. In order to be compliant with the rules and, at the same time, facilitate a pioneering, integrated approach, personal awareness and accountability was a critical success factor to navigate grey areas and still “do the right thing” in terms of compliance. Raising employee self-awareness helped to ensure that the company was conducting its business appropriately, while still working collaboratively with decision-makers and communities and allowing internal decision-making to be guided by what the external customers needed.

### **Collaboration with payers and patient reps is essential**

The patient- and customer-centric model extended across almost all aspects of the business, from designing the packaging to the medical teams’ interactions with physicians, as well as the engagement with academic, clinical, and regulatory bodies. The approach to two of the key communities—payers and patients—arguably gave the most significant pioneering results in terms of building a successful commercial launch that respected the integrity of all the communities involved.

#### **1. Collaborating with pricing authorities to accelerate positive pricing & reimbursement decisions**

To address the many pricing hurdles in a launch preparation, we initiated a program of individual dialogue with the pricing and reimbursement authorities in each individual European country. We used the dialogue to understand where the payers saw the biggest challenges in agreeing to pay for the new treatments, and how these could be overcome. The HQ teams built this feedback into the pricing and reimbursement strategy and materials. This resulted in an approach to pricing, provision of specific evidence that the budget holders needed, and the development of further data, where needed, in order to move the conversations forward—all of which was based directly on payer input. We were able to reduce times to positive reimbursement decisions across the launch markets, and in some cases, almost one year faster than the industry average.

#### **2. Collaborating with the patient community to create meaningful programs for the therapeutic area**

In well-defined rare diseases, the patient communities are represented by not-for-profit associations in a tightly knit community that is well-organized and structured. Funds, for a large part, come from companies developing and manufacturing therapies for the condition in question. This can create potential tensions, because companies might express a desire to influence which activities and programs the associations undertake, while the associations might feel pressured to follow the companies’ suggestions.

To engage the patient community on a customer-centric basis, the launch teams invested

in creating a real and very genuine dialogue with the community lead representatives. By diving deeper into what really mattered for the community, the organization discovered several areas where the patient representatives felt unable to initiate and develop programs that were of critical importance to them. That was because such programs did not give rise to “traditional” areas of publicity and, therefore, were not of sufficient interest for companies to fund. By identifying these areas and putting together programs of support that were driven by the patient needs rather than the company’s ability to participate or “brand” the offering, the team was able to forge a more meaningful approach to positioning the new therapies in the context of existing established treatment options.

Indeed, the approach to the payers was born of a request from the patient leadership, which expressed that one of its biggest concerns was that the new therapies would only reach “the privileged few.” Its guidance led to the payer outreach program mentioned earlier and an approach that was built on “pricing for access”—to secure that the new, first-in-class therapeutic options could reach as broad a community as possible.

#### **Competitive boost**

In our case, it could be argued that necessity drove a need to develop and deliver a patient- and customer-centric approach to commercialization. The company was relatively small, with no dedicated medical or sales force in place for the therapeutic area. It was a relatively unknown organization in the therapy area,



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The product launch landscape has seen some significant shifts. The more complex distribution model, new product types, and increasing influence of payers are just a few of the factors creating a more challenging landscape for product launches. Emerging biopharma companies must decide if they will go it alone to launch their product or look for a partner who has experience and resources.

In this session William McClellan and Maneesh Gupta will share a comprehensive analysis of drug launches to show how biopharma compare to large pharma launches, identify common launch archetypes based on market need and product differentiation, and share the framework to help you identify the archetype of your product and the critical success factors associated with that.

Key take-aways:

- Insights into how biopharma companies perform in today's launch environment
- Categories of launch archetypes and their correlation to first year revenues
- How to recognize your archetype and the critical success factors for launch

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seeking to enter a market dominated by large, well-established players. The launch was critical to the future of the company. Building on the drugmaker's rare disease legacy by identifying a genuine and sustainable patient- and customer-centric op-

erating model was a way to turn its small scale and newness in the field to its advantage.

Adopting this model meant that the organization was able to successfully enter and launch in an established competitive landscape and to win business from

a standing start and in a short time horizon. It also created an engaged and motivated workforce "with a heart." Most importantly, the approach helped facilitate earlier patient access to a more advanced and beneficial treatment. **PE**

## 'Centric' Forces

*Critical success factors in building and operationalizing a patient- and customer-centric organization.*

**1. Create a genuine focus on connecting with customer organizations and bringing their concerns and considerations as drivers.** This needs to come from the very top of the organization, guided and delivered from the CEO down. Having senior leadership participate actively in engaging with the community not only allows the strategy to be based on what they personally hear, but also sets the tone for the whole organization by prioritizing real interactions with the customer base.

**2. Create a shared "shared reality" that can serve as a rallying point for the entire company's way of working.** In this case, it was the patient and, given the nature of the rare disease field, this could literally be a real person who could serve as a "poster child" for what the entire organization was seeking to accomplish. Inviting patients and their families to present their stories to the organization at meetings reinforces that, especially for non-customer-facing roles. Having an explicit, shared, real-life, and personal mission helped people across the company to orient their efforts around what truly mattered. In day-to-day business, the shared goal could create alignment, facilitate integration, and defuse eventual tensions between departments, because participants could elevate beyond personal points of view or "turf discussions" and align thinking around a shared goal.

**3. Create the right profile for people who are likely to thrive and be successful in the organization.** Hiring the right people is a critical success factor for almost any business; however, it became clear that the profile to create and deliver a successful customer-centric business in a pharmaceutical company required a very specific and defined set of skills. Team members needed to be seasoned enough to be able to draw on experience and self-manage, rather than be directed in every interaction; they needed to have authenticity and a strong sense of self-reliance and self-delivery. In a larger organization, people might not be empowered to feel the same sense of personal accountability, which can lead to the feeling of being

a cog in a machine. In a small company, that places high reliance on every interaction with a customer, stakeholder, or decision-maker; personal accountability is critical.

**4. Create a culture where it is acknowledged that individuals and the company are doing things for the first time, where calculated risk-taking is expected and mistakes are perceived as learning opportunities.** Taking input from the communities might challenge conventional wisdom and may require the development of new pathways or tools where the organization does not have any experience. This means that pathfinding where no map exists—what might be termed "pioneering"—is a critical skill. It was vital to promote an explicit culture of openness and being "out of your comfort zone," where it is not only okay but necessary to take small, calculated risks by trying out new things. Sharing failures—including from the leadership team—at formal meetings and discussing lessons learned from what went wrong stimulated creativity and new approaches.

**5. Make desired behaviors and ways of working explicit within the organization.** Using company awards and "Town Hall" meetings as moments to call out, highlight, and recognize individuals or teams who have displayed the desired behaviors, and, critically, making explicit how these behaviors have contributed to the overall company mission and objectives was a key element of building the organization. The leadership team turned an existing company awards program into a way to show how behaviors could bring better business outcomes, rather than just being a feel-good moment.

**6. Use corporate objectives and incentives to drive collaborative engagement.** Starting at the executive leadership team level, the medical, commercial, and access functions had highly aligned objectives and were incentivized against similar goals. This needed to be tailored down in the organization, because medical staff in-country cannot be incentivized or bonused in the same way as other functions. However, at the C-suite level, the leaders had not only aligned, but shared goals. This embedded a culture of collaboration from the top down.



**WILLS**

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# Gaining Ground with Stem Cells

While the field of regenerative medicine has grown considerably since the '90s—in innovation and acceptance—entrenched companies such as Athersys are looking to forge new advances in the stem cell arena by transforming promising science into real-world treatments

By Lisa Henderson

If we've learned one thing, it's that science moves in mysterious ways. Science is more of an art than say, a science. How else can you explain the history of Athersys, and the journey of its co-founder, Dr. Gil Van Bokkelen? He received both a BA in Molecular Biology and Economics from the University of California at Berkeley, and a PhD in Genetics from Stanford University School of Medicine. But rather than practice medicine, Van Bokkelen says, "I didn't want to be the person to say, 'sorry, I can't help you.' I wanted to be part of the solutions." From there, he and his compatriots were wooed in the mid-1990s from the beauty and promise of the early biotech presence in San Francisco to the Midwest, where promising technologies developed in local academia were leaving. While Van Bokkelen and

Athersys co-founder Dr. John Harrington were not exactly thrilled at the prospect of a move to the Midwest, the opportunity was too great.

"We met a handful of people with a vision at Cleveland Clinic, Case Western University, and University Hospitals," says Van Bokkelen. The leadership at those institutions and in the local community were tired of seeing young entrepreneurial talent leave Ohio and move to the coasts, a phenomenon referred to as the "brain-drain." They decided it was time to create a magnet that would help attract, incubate, and retain entrepreneurs and innovative young companies, and made the commitment to work with the team from Stanford to establish a business incubator specifically designed for fledgling biotech companies—called BioEnterprise. Athersys was formed from those efforts.

The work that Athersys was doing back then was a prelude to the company's current focus on regenerative medicine. At the time, the founders of the company made international headlines by creating the world's first entirely synthetic human chromosome. This accomplishment was quickly overshadowed by the cloning of Dolly the sheep in Scotland reported in *Nature* in 1997. The scientists had produced a lamb named Dolly that was created from genetic material from an adult cell. However—along with a flurry of global reactions from the US, European Commission, and the Vatican—cloning itself continued, but proved inefficient and unscalable.

Fast forward 20 years, and the acceptance of regenerative medicine, which encompasses the fields of gene therapy, gene editing, cell therapy, tissue-engineering, and organ regeneration, has made major strides. FDA approvals for Novartis' CAR-T Kymriah and Spark Therapeutics Luxturna last year, along with clinical trials in other oncologic and rare diseases are paving the way in the larger regenerative medicine field. A recent report



Gil Van Bokkelen, Chairman and CEO, Athersys Inc.



indicates that the global regenerative medicine market was worth \$18.9 billion in 2016 and will grow to over \$66 billion by 2022, with a CAGR of 23.3% between this time frame.

But the stem cell area is one that features only a handful of pioneering innovators focused on transforming promising science into real-world treatments, and Athersys is one of them. The company addresses the stem cell scalability issue with MultiStem, described as an “off-the-shelf stem cell product that can be manufactured in a scalable manner, stored for years in frozen form, and administered without tissue matching or the need for immune suppression.” MultiStem has been in clinical trials for several therapeutic areas, including indications in the cardiovascular, neurological, inflammatory, and immune disease areas.


Athersys has received a lot of recent attention in the market for a spate of announcements, including an expanded deal with Japanese biotech Healios KK, which obtained exclusive licenses for the development and commercialization in Japan of MultiStem therapy for the treatment of acute respiratory distress syndrome (ARDS) and of MultiStem cells used in combination with iPSC-derived cells for the treatment of certain organ diseases. Healios also received an exclusive global license to develop and commercialize MultiStem cells, either as a standalone therapy or in combination with retinal pigmented epithelial (RPE) cells for certain ophthalmological indications, and an expansion of its license to use Athersys technology to support its organ bud programs to include other transplantation areas.

But one of the more promising areas for MultiStem, according to Van Bokkelen, is in stroke. He explained that the current standard of care—which is 20 years old—requires that the clot dissolving agent, tPA, be administered within three to four hours after the stroke event. That is a mighty small window for a stroke victim, and most patients don’t get to the hospital in time to receive treatment, especially when many are “wake-up” strokes, or individuals that have had “small” strokes that don’t necessarily have the patient heading to the hospital immediately.

The Athersys team believes that while the therapy is not actually fixing the stroke, it is addressing the overactive hyperinflammatory response that is now known to cause much of the permanent damage after a patient experiences the event. This overreaction is then followed by immune depression, leaving patients susceptible to a host of complications in the weeks following the stroke. As a result of the narrow time window for longstanding treatments, the lack of alternative therapies, and the extensive damage caused by inflammation in the brain, most patients that experience significant disability don’t recover, and may depend entirely on care from family members or professional care givers, or need full time institutional care for the rest of their lives. However, clinical data shows that MultiStem works up to even 36 hours after the stroke, to help patients progress past the initial disability and have better outcomes. Athersys has received fast-track status and regenerative medicine advanced therapy (RMAT) designation from the FDA for this indication.



This is also the theory behind a recently announced trauma trial that is being funded in part by the Department of Defense. Building off of promising preclinical studies, a Phase II clinical trial at The University of Texas Health Science Center at Houston will evaluate MultiStem cell therapy for early treatment and prevention of complications after severe traumatic injury. The study will be conducted at Memorial Hermann-Texas Medical Center, one of the busiest Level 1 trauma centers in the US. Doctors noted that following a serious trauma, an acute hyperinflammatory response is frequently triggered, which can impair recovery and lead to additional complications. They hope to provide more data that MultiStem responds to signals of inflammation and tissue damage by protecting injured cells, stimulating new blood vessels, and the recruiting of other cell types to promote tissue repair and healing to address the response and reduce complications.

Van Bokkelen says, “We are committed to conducting well-designed clinical trials for this cell therapy, with consistent safety profiles to address many unmet medical needs, and we are also proud of the environment and legacy of innovation that we helped create here in Ohio.” 

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# Opioid Litigation: Evading the Widening Crosshairs

The role of insurance and risk management in protecting middle-market distributors from the growing opioid MDL

A massive multi-district litigation (MDL) filed against pharmaceutical companies engaged in the production, marketing, and distribution of prescription painkillers is raising questions about insurance liability and who will ultimately be held responsible for the nationwide opioid epidemic.

Plaintiffs in the lawsuit are alleging that the manufacturers of prescription opioids “grossly misrepresented the risks of long-term use of those drugs for persons with chronic pain.” Distributors are also alleged to have “failed to properly monitor suspicious orders of those prescription drugs—all of which contributed to the current opioid epidemic” taking the lives of about 115 Americans per day.

What started as a lawsuit aimed at the largest manufacturers in opioids has expanded to include companies involved in nearly every stage of the supply chain, and middle-market distributors are far from immune. The MDL has ballooned to include hundreds of individual cases and dozens of defendants so far. Two lawyers I spoke to described the attorneys representing the municipalities, hospitals, third-party payers, union benefit plans, and Native American tribes named as plaintiffs in the MDL as “carpet-bombing” the industry by roping in as many companies as they can.

Many of the large pharmaceutical manufacturers and distrib-

utors named as defendants in the litigation were initially involved due to their marketing of branded opioid products. Most middle-market firms had no role in the marketing excesses alleged by the plaintiffs, but this hasn’t stopped plaintiffs from naming them in complaints.

Presiding Judge Dan Polster is seen by many as a social reformer who will use this case to take meaningful strides in the mitigation of the opioid epidemic. Many believe Polster is pushing to resolve this issue with a settlement that could leave the industry on the hook for billions of dollars in restitution and legal expenses.

Whether or not middle market distributors contributed to the widespread use of opioids, these companies are subject to the significant legal costs, business interruptions, and reputational damage that come with being named in the MDL. Making matters worse is that many of these companies may be more exposed than they previously thought.

## Understanding the insurance market’s response

Part of what makes this MDL unique is that most of the cases are not general liability cases that focus on bodily injury or property damage that typically trigger an insurance policy. Rather, plaintiffs are arguing it was intentionally malicious and deceitful behavior that led to the financial burden imposed on the local

municipalities that have been left to pick up the pieces today. As a result, many of the claims made in these cases do not include specific allegations that would trigger general liability policies and force insurers to address subsequent legal costs. In fact, I spoke with one lawyer representing several middle-market opioid distributors in the MDL who told me they are yet to see a single insurance policy be triggered as a result of this lawsuit.

One underwriter told me that insurers do not want to be “walking into a burning building.” Rather than leaving any room for policy language debate, some carriers have taken immediate, decisive action to insert outright exclusions for opioids and governmental actions into their policies. Others are attempting to exclude allegations involving opioid addiction, but may distinguish addiction and associated marketing actions, leaving the door open for claims resulting from design or manufacturing defects. Finally, some carriers are making distinctions to pare coverage back as it pertains to specific opioid exposures, including clinical trials, animal products, and newer products used exclusively in hospital settings. There is also a product identification issue for newer distributors that may be roped into the MDL despite having no involvement in the initial alleged marketing excesses of the branded opioid products that are at the center of this mass tort. This predicament could force an insurer to rely on a summary judgement to extract the distributor from the lawsuit, which puts insurers in a difficult position.

While reinsurance affordability and availability have also made underwriting this risk more

challenging, some insurers are still willing to consider it in some cases. However, securing a policy that meets the risk tolerance needs of the insurer while providing adequate coverage for the distributor will require additional negotiations and a more meticulous eye when reviewing the policy on behalf of both parties.

### How distributors can still protect themselves

This new insurance environment places companies in a tough spot. Insurers are examining their general liability policies very closely to protect themselves from any unnecessary exposure, and the policyholders must do the same by working with their brokers to understand how their coverage may be affected.

Distributors should also consider a number of risk management actions to reduce their liability. They can start by reviewing their legal and regulatory obligations as it pertains to their oversight of opioid orders. The Controlled Substances Act mandates that all DEA-registered entities distributing opioids must “design and operate a system to disclose ... suspicious orders of controlled substances.” It is imperative that distributors be able to demonstrate and justify the efficacy of their order monitoring systems to prove they’ve fulfilled this obligation—which may require upgrading or updating their reporting mechanisms.

Conducting and documenting a contractual review of relationships with manufacturers, doctors, and pharmacies to ensure that responsible prescription and distribution practices are maintained is prudent. Manufacturers, distributors, and other third-party contractors are also

held responsible for varying levels of oversight depending on their agreements with each other and pharmacies and doctor networks. Any opioid distributor with exposure in the current legal environment must take a close look at these documents to identify these obligations and ensure they are being fulfilled. These agreements also tend to contain indemnification provisions that are

**No matter their level of involvement in any accusations against the pharma industry, middle-market distributors must do everything they can to reduce their financial, operational, and reputational risk in the face of the MDL**

worth a close review as they have the potential to clarify and/or transfer a company’s culpability to someone with the greatest responsibility for the product while increasing their likelihood of securing an insurance policy.

Finally, distributors should take proactive measures to address the public opinion concerns surrounding opioid abuse. The MDL only serves to reinforce the public’s perception that the pharma industry is to blame for the opioid epidemic. Community outreach campaigns, partnerships with local advocacy groups, and communications programs aimed at educating doctor networks and pharmacies on the dangers of opioid use can align an organization as being part of the solution, as opposed to the problem.

### A new normal

No matter their level of involvement in any accusations against the pharma industry, middle-market distributors must do everything they can to reduce their fi-

nancial, operational, and reputational risk in the face of the MDL. While the current focus of the plaintiff’s bar may rest with the costs of abuse to municipalities, in time they may focus on individuals injured by such exposure or addiction to opioids. At that time, companies manufacturing or distributing pain medications and their insurance carriers may be in the bullseye. As such,

review of new allegations and careful reports of such circumstances to your product liability insurer may preserve liability coverage should a distributor become aware of specific injuries from such pain medications to patients.

This litigation could usher in a new normal in opioid manufacturing and distribution. That new normal could mean opioid manufacturers and distributors must comply with new regulations and practices to ensure effective marketing, communication, and safety practices are in place. A settlement could further impose such new standards and limits on business operations, resulting in additional requirements by distributors to take further preventive measures to ensure the safe distribution and consumption of these powerful drugs. By taking the right risk management steps and understanding the important role of insurance, companies can be better prepared to navigate impending litigation. **PE**

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# INDIA

## STANDING OUT FROM THE CROWD

“Over the past few decades, the Indian pharmaceutical industry has established itself as a global powerhouse for the production of bulk drugs and generics which have gained dominant market shares in the world’s most strategic markets and tremendously bolstered healthcare affordability and accessibility on all continents,” states Suresh Prabhu, India’s Minister of Commerce & Industry and Civil Aviation. “India is undoubtedly a significant player in the global marketplace, representing an important source of FDA-regulated products,” confirms Dr. Letitia Robinson, director of the India Office of the US FDA, which was set up in New Delhi in 2008.

Though perhaps lesser heralded, India’s critical role on the global pharmaceutical stage echoes the country’s ever-increasing significance in many other regards: to name only a few examples, the Center for International Development (CID) at Harvard University predicts that India will be the fastest growing country in the world for the coming decade, at 7.9 percent GDP growth, and its population could surpass that of China around 2024, according to the UN’s 2017 World Population Prospects. When it comes to the fine chemical and pharmaceutical industries, numbers are equally impressive: “with 573

approved facilities, India continues to have the highest number of US FDA-registered manufacturing facilities outside the US, while over 800 are UK MHRA approved and approximately 1,400 manufacturing units are WHO GMP (Good Manufacturing Practices) certified,” highlights Dilip G Shah, secretary-general of the Indian Pharmaceutical Alliance (IPA).

Thanks to the Indian ecosystem’s remarkable expertise in reverse engineering and its unrivalled capacity to provide health systems around the world with large volumes of affordable generic drugs, Indian pharmaceutical exports have skyrocketed from USD 3.9 billion in 2004 to around USD 17 billion today according to the Pharmaceuticals Export Promotion Council of India (Pharmexcil), while Indian companies make up 25 percent of the US generic market share. “From an Indian pharmaceutical perspective and as a country, we have shown a very high degree of capability to attain such market share. A question that I have asked myself is where do we go from here? Is it better to be growing by 45-55 percent or be entering other areas as well – such as the development of new molecules, biosimilars and biotechnology. I believe this is the next wave of the Indian pharma industry,” reckons Murtaza Khorakiwala, managing director of homegrown entity Wockhardt.

## SCALING THE VALUE CHAIN

As a matter of fact, pioneering domestic companies triggered this diversification phase more than a decade ago, and frontrunners have already begun reaping the rewards of their bold investments. “Intas actually started its biosimilar program around 12 years ago, and we have already launched 12 biologics in India. With the approval of Filgrastim in February 2015, we moreover became the first ever Indian company to launch a biosimilar in Europe,” proudly documents Binish Chudgar, vice-chairman and managing director of Intas, the largest privately owned Indian pharmaceutical company with sales of over USD 1.7 billion during the last financial year. “Moving forward, we would like to bring one or two of our biosimilars onto the global stage each year, while we are currently running six programs at the moment, mainly in oncology but also for autoimmune diseases. Overall, a large share of our resources are allocated to new chemical entities (NCEs) and biosimilar programs, as we want to ensure our Added-Value Products division makes up over 30 percent of our revenues within the next five years,” he adds.

In addition to biosimilar programs, prestigious Indian leaders have not shied away from the development of novel drugs and new biologics either. “Lipaglyn – India’s first NCE – has been granted investigational new drug status with the US FDA. Currently we have three Phase II studies in the US and another four in India. Non-alcoholic steatohepatitis (NASH), which is the indication for Lipaglyn we are currently working on, is an area of unmet healthcare need as there are currently no drugs approved for the treatment of the disease in both emerging and



**Suresh Prabhu, Minister of Commerce and Industry; Dr. Letitia Robinson, director, US FDA India office; Binish Chudgar, vice-chairman and managing director, Intas**

developed markets,” stresses Sharvil Patel, managing director of Zydus Cadila, India’s fifth largest pharmaceutical company.

While Biocon recently made global headlines when the US FDA approved its trastuzumab-dkst (co-developed with US-based Mylan), the Indian company is also pushing the development of groundbreaking biologicals. “Biocon’s itolizumab, specifically, is a very unique molecule as it is a ‘first in class’ biologic, a humanized recombinant anti-CD6 monoclonal antibody for the treatment of patients with active moderate to severe chronic plaque psoriasis. It harnesses a very different treatment pathway and boasts a novel mechanism of action. While India is not well known for novel drugs, we are trying to change that,” highlights Kiran Mazumdar-Shaw, chairwoman and managing director of Biocon.

In the meantime, Bharat Serums & Vaccines (BSV), a biopharmaceutical company with R&D units in USA, Germany and India, decided to develop the world’s first recombinant product in fertility, which would enable the elimination of variations typically encountered in urine-derived fertility injectable drugs, as all products will originate from the same cell line. “We are still enrolling patients for our Phase I clinical trials, which have been advancing at a very good pace. Leveraging recent technological advancements, I believe this first-of-its-kind product could moreover be reasonably priced and more consistent than urine-derived fertility products,” explains Bharat V. Daftary, chairman and managing director of BSV, which has also started the pre-clinical phase for two highly needed biologicals in the critical care arena. “I am terribly excited about these two products, which could save a large number of lives and have a game-changing impact in ICUs all around the world. In this regard, I am particularly confident in the skills and creativity of our California-based R&D center, where we develop all our cell lines before transferring them to and scaling up in India,” he relates.

## OUTSOURCED SERVICES: CREDIBLE PARTNERS

In the meantime, India-based companies have secured a place under the sun for themselves by partnering with leading American, European, and Japanese pharmaceutical companies for the discovery, development, and manufacturing of their products, including innovative drugs. “When looking at the macro environment,

### INDIAN PHARMA EXPORTS APRIL 2017 / FEBRUARY 2018

Indian pharma have grown by 2.43 percent to reach around USD17.25 billion for de period

#### TOP THREE REGIONS (IN TERMS OF ABSOLUTE VALUE)

REGION	FY 2018	CHANGE %
North America	4,831.5	-8.04
Africa	3,016.09	4.99
EU	2,464.08	7.65

#### TOP THREE REGIONS (IN TERMS OF ABSOLUTE VALUE)

REGION	FY 2018	CHANGE %
CIS	659.41	16.79
Other European Countries	136.94	16.59
Other America	45.46	12.6

Data shows exports from April '17 to February '18 in USD million and the change in value compared with year-earlier period

Source: Pharmaceuticals Export Promotion Council (PHARMEXCIL)



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all Big Pharma companies want to increase the speed-to-market of their life-changing products while at the same time reducing development and manufacturing costs. They strive to apply this approach to an ever-increasing number of products in the pipeline but they do not hold the in-house capacity to reach this objective. In this context, they are left with no choice but to look for external partners that can enable a streamlined and faster go-to-market model,” documents Vivek Sharma, CEO of Piramal Pharma Solutions (PPS), one of the world’s leading CDMOs with a presence in North America, Europe, and Asia.

“In the meantime, the overall number of biotech companies operating worldwide has increased tremendously over recent years, and the majority of them do not hold in-house development and manufacturing capacities either,” he adds. Again, the recent achievements of India-based Contract Research and Manufacturing (CRAM) companies and CDMOs are particularly impressive: for example, in 2017, the US FDA granted approval for Tesaro’s ovarian cancer drug, which Dishman will produce at its Bavla facility in Gujarat. “When the clinical trials of this drug were happening, Dishman was the API supplier alongside being a key supplier to Tesaro; now that this cancer drug has been approved the volume will jump significantly. Given the relationship and the trust that we have established over the years with the US FDA, they allowed us to start the supply of APIs to Tesaro already,” remarks Dishman’s chairman JR Vyas.

Over the past decade, India also witnessed the rise of niche, specialized service providers, which share the same focus on the most stringent pharma ecosystems in the world as their glorious predecessors. “I realized that there was no contract manufacturer dedicated to effervescent products based out of India or the US, which prompted me to found Vovantis in 2008. Today, 50 percent of our revenues come from the US, where we manufacture private labels for the main retail chains, and we can produce all effervescent products commercialized in the US market,” explains ASENCE Group’s managing director, Mohal Sarabhai.



**Sharvil Patel, managing director, Zydus Cadila; Kiran Mazumdar Shaw, chairwoman and managing director, Biocon; Bharat V. Daftary, chairman & managing director, Bharat Serums and Vaccines**

“In the meantime, we just started registering our effervescent products in the UK and expect to have our facility inspected by the MHRA shortly; once approved, we will use this UK base to expand into other European markets, while we are about to double our production capacity to sustain this vision,” adds Mohal Sarabhai, grandson of the illustrious scientist and industrialist Vikram Sarabhai, whose company Sarabhai Group was one of the first integrated pharmaceutical giants in India and the country’s market leader until the mid-1980s.

## THE ONLY WAY FORWARD

India-based service providers are also aiming to fully leverage the country’s R&D potential. “While we are a US-centric service provider, the fact that we are domiciled in India affords us a number of advantages - access to a rich pool of scientific talent, a relatively younger English-speaking work force and lower operating costs. For example, the rate at which India produces graduates with master’s degrees and PhDs in chemistry and biology is astounding, and it has allowed us to build up our own scientific talent pool at an eye-catching pace,” stresses Jonathan Hunt, CEO of Syngene International, one of the fastest-growing CRAM organizations in the world, which has



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## Piramal: Redefining the CDMO Relationship



**Vivek Sharma,**  
CEO, Piramal  
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As a leading player in a global CDMO industry shaped by a frenzy of M&A deals over recent years, the first and foremost objective of Vivek Sharma, CEO of Piramal Pharma Solutions (PPS), is to develop the company to make it as customer-centric as possible – and to be recognized by their customers for this commitment – rather than instinctively building up production capacities and capabilities. “Large or small, we look for acquisitions that

fit well with our needs: these would include expanding our geographical footprint, complementary or new capabilities that are synergistic, and technologies that fit well with our customers’ future requirements, to name a few. Overall, all our investments are conducted in a way that can bring more added-value to our partners,” he explains.

Besides guiding the company’s inorganic development, this overarching vision truly trickles down to all of its processes. “Some of our customer-centric initiatives have even inspired our current partners, who look at replicating these processes within their own operations. For example, we have set up a unique model to collect, analyse, and integrate customers’ feedback. As part of this program, the performance of our different sites is measured according to feedback given by our customers, which allows me to closely monitor our strengths and areas for improvement,” explains Sharma, who was named ‘CEO of the Year’ at the CPhI Awards in 2015.

Sharma assesses the evolving relationship between pharma companies and service providers thusly: “First of all, I want to highlight that the quality of this relationship is absolutely crucial, and both sides must acknowledge that we depend on each other. My perception is that only greater integration can usher in better outcomes for both parties.”

Despite increasing price pressure, it moreover seems that pharma companies do not disregard the added value generated by their partners either. “In some situations, we even could increase our prices because – as part of our company’s continuous improvement process – we proved ourselves as able to generate a higher value for our customers, which they fully acknowledged,” he reveals.

However, capital constraints, reduced internal bandwidth to drive development projects, and a need for reducing costs and clinical timelines are realities in the new pharma world which partners like PPS also strive to address. “As a CMO we continue to look at creative alliances and innovative business models, which may include: pharma site divestiture to a CMO with committed volumes for a set number of years, risk-share models that reduce upfront costs, with potential for a higher payout for the CMO, on success tied to milestone events, and fixed price early development projects,” he concludes.





**Murtaza Khorakiwala,**  
managing director,  
Wockhardt

forged strategic partnerships based on dedicated, India-located R&D centers with BMS, Abbott, Baxter, Amgen and – more recently – GSK. In the same vein, Sharma of PPS confirms that his company is “today able to deploy cost competitive R&D-driven projects in India, because talent and structural resources are more largely and easily available than some years ago.”

“In this regard, we would like to see a better alignment between the government’s R&D vision and the concrete tools and means that it brings to the table, especially when it comes to dedicated incentives. As a matter of fact, the government recently reduced the weighted tax deduction on R&D expenses from 200 percent to 150 percent as part of the Budget 2018, which is difficult to understand given our country’s ambitions in the high-tech field,” bemoans Sameer Hiremath, CEO and joint-MD of the CDMO Hikal, whose





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Group

R&D center was built under the supervision of Lonza's former chief technology officer, Dr. Helmut Rupp.

"In a global context marked by increasing price pressure and decreasing margins, we foresee that companies holding basic technologies and still focusing on low added-value products will struggle to comply with rising quality standards. The only way forward is to continue climbing up the value chain and stimulate companies' innovation drive - and we are doing this with over 20 percent of our employees who work in Research & Technology," reveals Hiremath.

## ADJUSTING TO A NEW NORMAL

Indian pharmaceutical exports have grown more than five-fold over the past two decades, but the increase only reached 2.5 percent during the fiscal year ending March 31 2018, according to Pharmexcil. More worryingly, the value of Indian pharma exports to North America dropped by 8.04 percent to USD 4.83 billion during the 11 months up to February 2018. North



**Dilip G Shah,**  
secretary general,  
IPA

America, including the US, contributes to over 30 percent of the India's overall exports in terms of value.

"The last two years have been slightly turbulent because of policy changes and the pricing challenges which caused a certain level of disruption," confirms Zydus Cadila's Sharvil Patel. "With regards to price erosion in the US generics business, I believe that the latter follows a cyclical model and will therefore be corrected within three to four years, based on a supply and demand logic. As prices continue to decrease, manufacturing plants shut down, which nurtures the drive for M&A deals," notes Chudgar of Intas. While price erosion in the US generics market was in excess of 15 percent in 2017 and will perhaps be at similar levels in 2018, it is particularly difficult for Indian companies to cope with current price erosion, as they have to ship their products from India to the US. "Making this model sustainable and competitive requires large inventories, which explains why Indian companies have been badly hit by erratic pricing in the US, the number one export market for the Indian pharmaceutical industry," adds Chudgar.



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In the meantime, prices of raw materials (including APIs and intermediates) from China have been skyrocketing over recent years, thereby generating an even more complex equation to solve for domestic generics companies, which are over-dependent on imported raw materials, especially from China. “The prices of API intermediates have been increasing substantially, which created a supply crunch for API intermediates. The latter has automatically impacted the price of pharma APIs, which will – ultimately – increase generics prices in the US market,” highlights Chudgar, before warning: “Looking forward, I nonetheless believe that the margins that Indian manufacturers enjoyed before the beginning of the current cycle are definitely gone.”

In this ‘new normal,’ Indian formulation companies are left with no choice but to rationalize their US portfolios, further streamline their operations and strengthen their vertical integration in parallel to the long-term development of more complex, higher margin products. “In the US and European markets, it is not simply pricing that will increase market share; ability to respond to market needs faster than others will be more important. While some of our competitors in the US market operate with a 2000-product-portfolio, a company like Laurus with strong R&D and manufacturing capacities but only 50 stock keeping units (SKUs) stands as a very agile player.

Furthermore, we plan to fully leverage our company’s vertical integration as well as our proven capacity to generate higher margins than most of our competitors in the API sphere to thrive in the highly competitive formulation market, in spite of rapid price erosion,” explains Dr. Satyanarayana Chava, founder and CEO of Laurus Labs, one of the world’s leading API companies, which recently started selling HIV formulations in the US.

## **SURVIVING THE RAW MATERIALS ROLLERCOASTER**

The abovementioned price surge for raw materials actually came after a devastating phase of downward price pressure driven by China-based manufacturers which took over the global market and rendered many India-based companies unable to compete. “At some point, India’s power cost for the manufacturing of fermentation products was roughly equal to the final selling price of Chinese fermentation APIs,” reveals Mohal Sarabhai, managing director of the ASENCE Group and head of fermentation-focused API manufacturer Synbiotics.

This fierce competition has shaped – in many product categories – a new global landscape where few intermediates and API producers outside China have survived this spiraling price context. “For example, only two companies based outside China still supply Vitamin D3 in



**Mohal Sarabhai, managing director, ASENCE Group; Satyanarayana Chava, CEO, Laurus Labs**

2018, and India-based Fermenta is one of them,” reveals Satish Varma, managing director of Fermenta Biotech Ltd., one of the world’s largest producers of Vitamin D3. However, the India-based companies that survived those years of fierce price competition today are in a very interesting position. “In this context, our company has emerged as a very attractive partner for international customers eager to diversify their sources of supply and not exclusively rely on China-based producers,” confirms Satish Varma of Fermenta Biotech, whose production volume has increased 10 times from 2005 to 2017.

While intermediate and API prices have been surging again recently as China strengthened its control of pollutions norms, one might think that new Indian players will swiftly re-enter the global market and vie for a piece of the pie held by Indian ‘survivors.’ “Although India’s fermentation capacity is today clearly



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## Hikal: Carving out a Niche



**Jai Hiremath,**  
founder and  
managing  
director, Hikal

*Jai and Sameer Hiremath of Hikal document the company's specialty focus in the consolidating CDMO industry and articulate how Hikal is reinventing itself and climbing up the value chain.*

**Given the on-going consolidation shaping the CDMO industry, what makes you believe that a large mid-size company like Hikal can continue thriving in an industry context increasingly dominated by huge players?**

Jai Hiremath (JH): The consolidation shaping the CDMO sector will undoubtedly continue in the coming years, as these companies look at generating economies of scale. As per Hikal, we are not particularly worried by this industry trend, as the demand for our products and services is still particularly strong.



**Sameer Hiremath,**  
CEO and joint  
managing  
director, Hikal

Sameer Hiremath (SH): Economies of scale do matter, but one should not overlook the importance of specialty companies holding differentiated technologies.

In this regard, we see some Europe-based, mid-sized CDMO companies with a specialty focus that have been doing really well, so it also proves that there is a room for niche players like us with a unique expertise and technology. Customers are becoming more and more demanding, and the latter aim to partner with the world's best providers for a very precise part of the development and manufacturing process of a given molecule. In this

context, we believe that a company like Hikal, which aims to position itself as one of the leading companies in the world in its own areas of expertise, clearly holds opportunities for growth moving forward.

In the meantime, we decided to increase the R&D efforts conducted in Hikal's R&D center, with the objective of developing our own generic AI and API portfolio, both in crop sciences and the pharmaceutical business. Since 2015 we have filed a substantial amount of Drug Master Files (DMFs) with the US FDA, while we follow a life cycle extension strategy, where we focus on products that are about to go off patent.

**Where would you like to see Hikal in the next five years?**

JH: We want to maintain an annual growth rate of 15 to 20 percent, in line with our performance over the past five years. Fuelling our R&D pipeline will be absolutely crucial to fulfilling this objective, which will require more and more investments dedicated to this specific field. To ramp up this process and increase our chances of success, we look at joining forces with companies that can help us improve our capacities and strengthen our company's knowledge in some specific areas, such as continuous manufacturing.

SH: Our ambition is also to come closer to our customers: leveraging our strength in APIs & AIs. As you know, actives make up a large share of finished products' costs, and some customers have been asking us for quite a long time already to cover the entire value chain including formulations. At this time, we have ample opportunities to support our customers on the development and supply of actives in both our businesses while we continue to evaluate opportunities on a select basis for adding further value to our products.

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underdeveloped as a large share of domestic companies could not sustain the downward price competition triggered by China-based companies, India's stringent environmental framework for fermentation-centered API companies has so far prevented new players from rapidly entering this business again. As a result, Indian 'survivors' still hold a true competitive advantage," highlights Mohal Sarabhai.

## NO MISTAKES ALLOWED!

Another issue that has been grinding the gears of the Indian industry over recent years concerns quality compliance. "In India, pharmaceutical companies have had mixed success in upgrading their quality systems, and the number of warning letters from the US FDA to Indian manufacturing sites has increased in the last five years. While the proportion of official action indicated (OAI) and voluntary action indicated (VAI) decisions in US FDA inspections has remained the same (around 65 percent), the number of inspections increased by 30 percent in 2015. That same year, when some of our members received warning letters from the US FDA, it came as quite a surprise," relates Dilip G Shah of the IPA, before adding: "we did not, however, take the view that India and Indian companies were



**Satish Varma,**  
managing director,  
Fermenta Biotech

being targeted as we had a fairly positive relationship with the US FDA."

"Our risk-based site selection model focuses on drug manufacturing establishments, rather than countries," highlights Dr. Letitia Robinson, director of the US FDA India Office, while stressing that the problems encountered by the FDA's investigators in India are similar to those seen around the world in manufacturing: "common issues include inadequate or poor quality systems implementation, data integrity issues, inadequate validation of various processes used in manufacturing or testing, and product contamination," she adds.

"The level of regulatory scrutiny that a pharmaceutical company has to cope with often depends on the significance of its market share in the relevant country – especially when it comes to the US FDA. In this regard, it truly makes a difference whether a company holds only a handful of products or ships 50+ INNs from a given plant; when holding a small market share, regulators would typically not go into full details, but compliance inspections suddenly reveal themselves extremely stringent and



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## Maneesh: Ahead of Its Time



**Vinay Sapte,**  
managing  
director,  
**Maneesh  
Pharmaceuticals**

In the early 2000s Maneesh Pharmaceuticals engaged in a series of more than ten joint ventures and acquisitions in strategic markets - including the US, the UK and Brazil - at a time where most Indian manufacturers contented themselves with more basic export strategies. Interestingly enough, an ever-increasing number of Indian exporters are now aiming to replicate Maneesh's pioneering approach. "Indian exports have been recently plateauing – especially in key markets, while very few domestic companies' plants have been spared US FDA warning letters or export bans. When adding these aspects to increasing competition and foreign governments' push to foster the local production of medicines, one understands that Indian exporters are left with no choice but to

evolve their international strategies," explains Vinay Sapte, founder and managing director of Maneesh Pharmaceuticals.

"Although the 2008 Global Financial Crisis (GFC) and the worldwide economic downturn it generated had a harsh impact on our operations, we have gained crucial insights in terms of forging competitive, cross-border alliances; setting up, acquiring and running overseas plants; defining joint ventures' structures and business models; and protecting ourselves from variations of foreign currencies," he continues. As a matter of fact, all joint ventures set up by Maneesh around a decade ago – such as Tillomed, a Top Ten generics player in the UK market - have been flourishing, although Maneesh was eventually forced to divest its stakes along the way because of the financial turbulences generated by the GFC. "We are now on the brink of kick-starting a new international phase for Maneesh, while two of our Indian plants were successfully inspected and approved by the US FDA in 2016. In the meantime, we are putting a special emphasis on our R&D strategy and look at developing products specifically targeting the US market, as well as in licensing branded products with a high potential in developed markets," he adds. While Maneesh is now looking for distributors to partner with for the marketing of these selected products, the company's overarching vision is to follow the way it paved ten years ago: to become an integrated pharmaceutical company in strategic foreign markets. "This approach clearly emerges as the only way to be profitable in today's industry context," concludes Sapte.

in depth once a company has a substantial position," considers Chudgar of Intas. In the meantime, recent inspections seem to indicate that stringent regulatory scrutiny has been broadened to encompass API manufacturing plants, in addition to the formulation plants primarily targeted in the first place.

"I see quality compliance as a learning curve, while one should bear in mind that regulatory standards are also constantly evolving. Across our multiple manufacturing plants, Intas has successfully passed 50+ US FDA inspections over the past two decades, and the US FDA inspects one of our plants every six months on average," he adds. As part of the findings of IPA's Quality Forum - set up in 2015 with the vision of helping the Indian pharma industry achieve excellence in quality - progress has evidently already been made over the past three years: while Indian manufacturers accounted for 50 percent of all warning letters issued by the US FDA to non US-sites in 2015 – Chinese sites making up only 13 percent of the total – this number decreased to 29 percent in 2017 for India-based sites and grew to 35 percent for China-based sites.

In the meantime, regulatory and compliance issues do not seem to have utterly cooled down the eagerness of leading international companies to acquire India-based manufacturers and/or service providers, especially in very





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sophisticated product areas. For example, Swedish CDMO Recipharm completed the acquisition of India-based CDMO Kemwell in 2016 and acquired a majority stake in Nitin Life-sciences, an Indian sterile injectables CMO.

## A TOP-DOWN ENDEAVOR

In a context where even well-established, multi-billion-dollar domestic companies have received warning letters from the US FDA, quality compliance has clearly become strategically important across all layers of Indian organizations, including formulation and API companies as well as both B2B and B2C players.

“My approach is extremely simple: quality is everyone’s responsibility. As a matter of fact, it has been integrated as a Key Result Area for all of our 4,000 employees, regardless of the function they hold,” explains Vivek Sharma, CEO of PPS, which displays one of the best track records in this area. “You truly have to ensure that from top to bottom everyone understands that integrity, ethics and compliance are binary: they are either maintained or they are not,” confirms Jonathan Hunt of Syngene International.

“In this regard, I believe that quality compliance truly comes as a top-down endeavor, which has to be generated by the company’s heads before flowing throughout all layers of the organization. Indian CEOs with global aspirations know that they cannot take any shortcuts when it comes to quality standards and regulatory compliance, but the trickiest part is to convey and nurture this approach to their teams: in a vast and highly populated country like India, the paramount importance of quality and regulatory standards might not be obvious to all layers of our population,” adds Satish Varma of Fermenta Biotech.

When it comes to the overarching goal of avoiding regulatory and compliance issues, Indian CEOs may benefit from the cross-border, collaborative spirit that has been gaining traction across the country’s pharma ecosystem. “We assist and train

both Indian regulators and the Indian pharmaceutical industry on developing and maintaining the quality, safety and effectiveness of medical products, which includes addressing regulatory compliance issues. In this regard, Indian regulators have become important strategic partners for the US FDA, we regularly engage with them and also aim to build confidence in each other, develop quality standards and bilateral initiatives,” reveals Dr. Letitia Robinson of the US FDA India Office. “In an effort to adopt the best regulatory practices implemented in the world’s most advanced ecosystems, we closely and regularly interact with our peers from the US FDA, UK MHRA, Health Canada, and the WHO – among others. We are closely working towards capacity building, training, networking and knowledge sharing with the US FDA through one-to-one meetings conducted on a regular basis,” highlights Dr. Hemant Koshia, commissioner of FDCA Gujarat, the regulatory authority of the state of Gujarat.

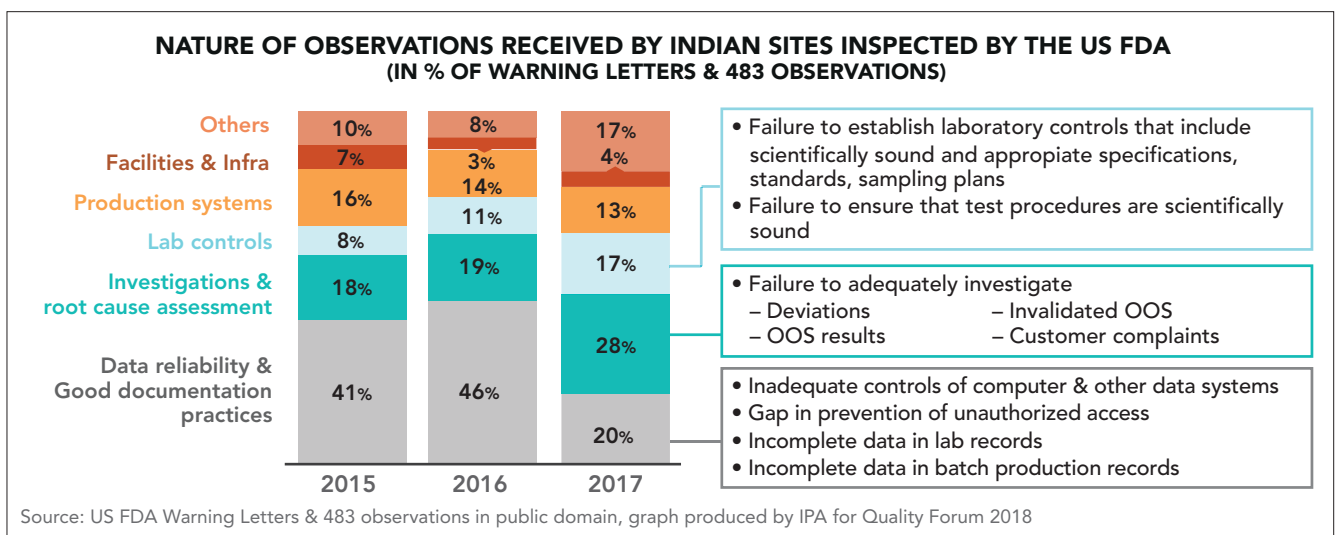


**Umang Vohra,**  
managing director  
& global CEO, Cipla

## MADE IN GUJARAT

The state of Gujarat’s regulatory authorities have made great efforts in terms of quality compliance and international harmonization. This is especially important as the Western state proudly stands as a pharmaceutical hub of global relevance, accounting for over 33 percent of India’s pharmaceutical turnover and 28 percent of its pharmaceutical exports.

“Gujarat’s history of manufacturing fine chemicals and pharmaceutical products goes back more than 110 years. Furthermore, the LM College of Pharmacy in Ahmedabad was established in 1947 – the year marking the independence of India – and therefore stands as the oldest pharmacy institute in the



## British Biologicals: Building, Consolidating, Expanding



**Dr. V S Reddy,**  
founder and  
managing  
director, British  
Biologicals

Although India has today emerged as a fast-growing nutraceutical market, the context was completely different when VS Reddy first established British Biologicals – now India’s leading nutraceutical company – in 1988. At that time, the Indian market was still at a very nascent stage, and the main challenge he faced not only concerned the limited purchasing power of the Indian population. “As one of the pioneers in the Indian nutraceutical market, we truly had to educate the domestic ecosystem and convey the crucial role played

by nutraceuticals as complements to allopathic treatments as well as powerful prevention means. Fulfilling this endeavor was no bed of roses: it took me almost ten years before the Indian physician community steadily began integrating our products in their daily practices,” explains Reddy, who is fondly known as ‘The Protein Man of India.’

Despite dealing in nutraceuticals, British Biologicals has adopted a promotional approach similar to that of any specialty pharmaceutical company selling science-based, prescription products. Reddy posits, “As we are above all a science-based company and all our products’ benefits and innovations are scientifically proven and evidence-backed, we have historically con-

centrated our efforts on general practitioners in a country where the latter’s guidance and prescriptions are strongly respected by patients.” He continues, “Moreover, Indian regulators have become extremely stringent with regards to packaging and marketing standards, ruling out nutraceutical products boasting unproven added value from the market.”

Leveraging its leadership in India and the uniqueness of the company’s brands, Reddy has initiated an aggressive internationalization strategy over the past two years and British Biologicals today exports its products to 35 countries. “We just opened an office in the US, where we are already supplying vitamins to leading retailers such as Amazon. Although the US probably stands as one of the most competitive nutraceutical markets in the world, it undoubtedly is a science-driven ecosystem, which should fuel the growth of our portfolio,” he says, while the company is ready to duplicate some of the clinical trials already conducted in India to fully showcase the added-value of its products to US stakeholders. “We believe that our unique diabetic diet, hepatitis syndrome, and menopause syndrome products could rapidly conquer substantial market shares in the US, and we will most likely concentrate our promotion efforts on dieticians operating in private clinics to propel these products’ market uptake,” he says, before stressing he is also considering several acquisition opportunities in the US and the UK to access overseas manufacturing capacities and support British Biologicals’ marketing strategy.

country,” posits FDCA Gujarat’s Hemant Koshia. It is also the state of origin of the Sarabhai Group, one of the first integrated pharmaceutical giants in India and the country’s market leader until the mid-1980s, which was initially set up in the 1950s by the illustrious scientist and industrialist Vikram Sarabhai through an exclusive partnership with ER Squibb and Sons, whose company eventually became part of the modern pharmaceutical giant Bristol-Myers Squibb. Sarabhai subsequently forged partnerships with Germany’s Merck KGaA and Swiss-based JR Geigy, which, after mergers with other Swiss-based companies CIBA and Sandoz Laboratories, gave birth to Novartis.

Gujarat today gathers together over 4,000 manufacturing licensees and industry heavyweights such as Torrent Pharmaceuticals, Zydus Cadila, Intas, and Dishman are headquartered in the state, which moreover accounts for 40 percent of the country’s CRAM companies and CROs. In terms of the reasons for this clusterization in Gujarat, Mohal Sarabhai of ASENCE Group notes that “First and foremost, Gujarat holds extremely good universities, especially in the pharmaceutical and medical fields, and infrastructure as well as a great labor force. Furthermore, it has become increasingly difficult for company heads to bolster a healthy dialogue with labor unions in the state of Maharashtra (where Mumbai is located) and in Northern India (where Delhi is located). Moreover, land is easily available and reasonably priced in Gujarat, which marks

a true advantage in comparison to the aforementioned states.”

Another important factor in Gujarat’s success is the fact that between 2001 and 2014, the state had a very dynamic chief minister – Narendra Modi – who ascended to the position of prime minister in 2014. This has contributed to raising the state’s international profile and attractiveness through the biennial investors’ summit, ‘Vibrant Gujarat,’ which makes it easier for Gujarati entrepreneurs and CEOs to convince international partners of their state’s investment potential.



**Dr. Hemant Koshia,**  
commissioner, Food  
and Drug Control  
Administration  
Gujarat

## NO PLACE LIKE HOME?

In parallel to their astounding expansion on the international scene, domestic companies have also strengthened their grip within India and today enjoy a 77 per cent share of the Indian pharma market, while only 18 multinationals emerge in the Top 100 ranking. In the meantime, India has remained a critical market for some of the most successful Indian players globally: Sun Pharmaceuticals, the fifth largest global specialty generic company, makes around 26 percent of its



USD 4.5 billion gross sales in India, where it stands as the market leader – and similar numbers apply to other domestic heavyweights. “There is a lot of energy being spent in trying to make sure that the Indian market lives up to its promise – as you know it is a USD 36 billion market and Cipla is aiming to reach USD two billion in terms of sales in the country,” testifies Umang Vohra, managing director and global CEO of Cipla, the third largest pharmaceutical company in India.

“More and more Indians can afford medicines which, in turn, increases market penetration, while there is a more conspicuous amount of consumption that goes into tier two, three and four cities. Hospitals have reached a certain standard of care and we see patients increasingly using hospitals to get treated,” continues Vohra. “I am positively impressed by the amount of time that local medical doctors give to their patients and to follow up. This is even more impressive as Indian doctors manage to attend up to a hundred fifty patients a day (versus ten to 40 patients a day in most other countries), thanks to efficient organization, anticipation, and adequate team structure,” adds Dr. Georges Jabre, the recently appointed CEO of Serdia Pharmaceuticals (India) Pvt. Ltd. (an affiliate of the Servier Group). “As very few external observers actually know this fact, I would also highlight that Indian hospitals do offer holistic care: healthcare professionals typically provide chronic diseases patients with a basket of exams, treatments and follow-up options – at various levels of costs, which are calibrated to the patients’ ability to pay,” adds Jabre.

“Last but not least, there is a favorable environment in terms of the policy context that generates access – price controls are one way to generate greater coverage,” expresses Cipla’s Vohra, while about 20 percent of the drugs manufactured in or imported to India are under price control based on the National List of Essential Medicines prepared by the Ministry of Health and Family Welfare. “Recent changes in pricing ensure that the market remains dynamic and the pressures on industry are running high, but ultimately it is the patient that matters and that is why we have made ‘going beyond the pill’ a strategic priority for the future,” recounts Venu Ambati, managing director of Abbott India. However, he is quick to point out that ‘affordability’ should not be dealt with in isolation, but rather as part of a comprehensive, holistic strategy. “We also need to focus on improving the other ‘A’s of the system – that is ‘accessibility’ and ‘availability,’” he muses.

In this regard, Finance Minister Arun Jaitley recently announced a new, ambitious National Health Protection Scheme, which will provide a health insurance cover of INR 500,000 [USD 7,800] per family per annum and cover more than 100 million vulnerable families, especially in rural areas. One still needs to see how and at which pace this ambitious scheme will be put into motion, but the Indian Government has so far proven itself particularly reliable when it comes to reform implementation. “In this regard, we also hope that the government will set up dedicated purchasing schemes for essential products, including for biologicals. For example, some areas of India are particularly affected



Venu Ambati, managing director, Abbott India Ltd; Georges Jabre, CEO, Serdia Pharmaceuticals (Servier India); Deepak Sawant, minister of health and family welfare for Maharashtra state

by snakebites, but public hospitals do not have antidotes,” regrets BSV’s Bharat V. Daftary. Roughly 46,000 people die of snakebites in India every year, according to the American Society of Tropical Medicine and Hygiene, accounting for nearly half of the 100,000 annual snakebite deaths the world over.

“As India remains essentially a self-pay market, patients are also much more demanding – towards the doctors and the medicines prescribed – than in countries with established social security systems. Therefore, pharmaceutical companies must be more precise when it comes to detailing the benefits of their medicines as well as in their overall communication to external partners,” reveals Serdia’s Jabre. “Furthermore,



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operating in today's environment implies being extremely focused, as the time available for doctors' visits is on average shorter as compared to previous years. Indeed, as most patients are favoring the private sector, doctors are giving us less time to develop our ideas and services – hence the importance of being sharper as a company if we want to convey our undeniable expertise," he continues. While affordability is first and foremost driving the Indian market, it nonetheless does not mean that physicians don't acknowledge the added value brought by pharmaceutical companies. "We for example developed a new dosage form of enoxaparin enabling self-injection through a multi-dose pen and became the first company in India to market such technology in this product category. Although competitors swiftly started copying our pen, gynecologists remained loyal to our product, because they trust our company and value its expertise," explains Daftary of BSV, which currently ranks third in India's gynecology market and aims to shortly reach second position.

## THE RIGHT FOCUS: PARTNERSHIPS

In the consolidating Indian market where the top three companies hold a 19 percent market share and the top 50 companies make up 84 percent of the market, an ever-increasing number of players are embracing a specialty approach. As part of this strategy, forging partnerships with international companies and bringing to the domestic market products and technologies that are not yet available locally stands as a great opportunity that cannot be overlooked. "We have already signed in-licensing partnerships with European and US companies, and these products will most likely reach the Indian market within the next three to five years," reveals BSV's Daftary.

The same thinking also drives leading multinational companies operating in the country, which want to leverage the exceptional coverage network of domestic companies to expand access to innovative medicines. "We have a commercial partnership with Lupin for the promotion and distribution of several Lilly products in our diabetes portfolio," highlights Luca Visini, the recently appointed managing director of Eli Lilly for India, while similar partnerships have been multiplying at an impressive pace over the past months. "Although Cipla was one of the companies that fought against multinational patents in India, we are today the preferred partner for multinational companies," explains Cipla's Vohra to illustrate the wind of change blowing through India's pharmaceutical market.

"Finally, in our vision, partnerships will not only encompass the commercial sphere, and – given our huge ambitions in India – we truly aim at embracing all layers of the country's healthcare system, whether it concerns medical universities, the union and state ministries of health," stresses Serdia's Jabre, while India's 29 states and seven union territories form a fragmented healthcare reality with diverse epidemiological, cultural, climatic, and economic profiles but a similar eagerness to benefit from the



**Luca Visini,**  
managing director,  
Eli Lilly and  
Company India

industry's expertise. "We look forward to partnering with pharmaceutical and healthcare companies and jointly shifting the healthcare paradigm in India's second most populated state, whether it relates to prevention, treatment or the management of our healthcare capacities and centers," concludes Dr. Deepak Sawant, minister of public health and family welfare in the Government of Maharashtra, "a state where over half of the 112 million inhabitants exclusively rely on the State Health Department to access healthcare services and products," he points out.

## LEVERAGING THE PAST TO BUILD THE FUTURE

"Overall, India accounts for almost 20 percent of the global disease burden; moving forward, its thriving pharmaceutical market should benefit from the recently announced increase of public health spending, while the dynamism of our country's economy will undoubtedly contribute to cement the crucial importance of India in the operations of all pharmaceutical companies with global ambitions," believes Minister of Commerce & Industry Suresh Prabhu.

Whether it relates to the domestic stage – characterized by a huge growth potential but a limited pricing power – or to international markets shaped by soaring competition, sweeping trade policies, and regulatory scrutiny, the challenges that lie ahead for Indian companies are only matched by the bountiful opportunities that are still yet to be seized. "I however believe it is clearly easier for businessmen of my generation to reach our growth objectives: our predecessors have done an incredible job in convincing leading multinational companies that they can rely on Indian partners and suppliers. A few decades ago, entrepreneurs had to sell 'Brand India' even before selling their own company..." comments Hikal's Sameer Hiremath. "In the meantime, the new generation will have to be more innovative than ever, while reaching out to new geographies – such as Latin America and South East Asia – and diversifying revenue streams," assesses his father Jai Hiremath.

Finally, when it comes to further strengthening its significance within the global pharmaceutical and healthcare landscapes in the years to come, the Indian industry will undoubtedly be able to leverage a particularly precious asset: experience. "Through the challenging early years, we have learnt how to get the best returns on investment, and this expertise will be extremely useful moving forward," expects Binish Chudgar of Intas, whose sales grew from USD 100,000 in 1994 to over USD 1.7 billion in the last financial year. "This aspect actually does not exclusively apply to me or to Intas, but to all Indian CEOs that successfully developed their companies before India became a respected and dominant player in the global pharmaceutical market," he concludes. 🌟

**C**BI's Pharmaceutical Compliance Congress recently convened a diverse and insightful panel to reflect on the state of the compliance role within the pharmaceutical industry. There were several key messages—all invariably leading back to the challenges and opportunities of securing an effective place at a drug corporation's executive table.

Unlike the dog who one day catches the car, this goal is not about the chase. The prize here is of utmost importance: the opportunity to build and maintain company value and reputation with key stakeholders, including patients, investors, regulators, and employees; no small task and no small reward.

This is, in essence, a corporation's business case for quality—which compliance is a part of. Quality has been defined by many in different ways. Often times when someone says “quality,” others think “compliance.” But there is a difference.

As pioneers of quality management, Joseph Juran defined quality as “fitness for use;” Philip Crosby referred to it as “conformance to requirements;” and W. Edwards Deming essentially said that cost goes down and productivity goes up when quality goes up. In total, quality resonates as something that involves people, processes, performance, and expectations—including those of key stakeholders—and, hence, is much broader and more strategic than compliance.

There's no doubt that clear and relevant policies and procedures are necessary in navigating compliance risks. But that's only the starting point. All large multinational and most smaller organizations have world-class systems in place.

Yet, compliance issues still

## A Seat at the Strategy Table

How navigating compliance risks requires so much more than policies and procedures

arise, some even resulting in consent decrees or corporate integrity agreements, damaging company value and reputation sometimes beyond repair. Why? Navigating compliance risks requires so much more than policies, procedures, and even a seat at the executive table.

Let's build on the recent panel discussion with the following quality-related strategies:

- **Quality and compliance are not spectator sports.** Having someone with a seat at the big table is a ticket to the game. But more than a seat is required for effectiveness. Direction, ownership, and accountability all start at the top of the organization. But for a company to be successful in navigating compliance risks, everyone—not just the compliance officer or department—must have a role with clear responsibilities and expectations.


- **Anticipating, identifying, and resolving potential issues.** How well do you understand your risks and how well are you taking proactive measures to prioritize and mitigate those risks (e.g., working cross-functionally to break through silos) to fully integrate with your business plan? Having the right people with the right expertise and foresight involved in early and ongoing risk assessments is essential.

- **Building mutual trust and respect – Secret Sauce #1.** Unexpected issues will always arise. But that's not the time for building relationships. For those messy situations, it is paramount to have transparent and collaborative working

relationships already ingrained internally with third parties and with key stakeholders so that conflicts can be raised and resolved quickly and effectively to minimize potential damage to value and reputation.

- **What and when to invest – Secret Sauce #2.** Every organization faces the same challenge of limited resources and even less time. As such, compliance needs often are put on hold. So, with everyone vying for a piece of the same budget, it becomes critical that quality/compliance is able to effectively justify what and when to invest in the context of the overall business plan. Being able to project the return on that investment almost always beats the costs of non-conformances.

- **Alignment of rewards, recognition, selection, and promotion.** Culture can be defined as what's done and not done, what's said and not said, and the resulting consequences. So, in considering the role of corporate culture in navigating compliance risks, remember that what gets rewarded gets done.

Regulations and legal interpretations are always evolving in the fast-paced world of innovative life sciences. Navigating compliance risks requires so much more than policies and procedures. For the large pharma player or the startup, it involves all of the strategies mentioned and more to get out in front of potential issues before they become significant pain points—thereby creating a competitive advantage for the business and more predictability and confidence for the key stakeholders. 



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