Denise Myshko

Building a *Culture* of INNOVATION

Pharmaceutical R&D is under pressure to counter rising costs, depleted pipelines, and impending patent expiries. The industry is facing not only a productivity crisis, but also a crisis in innovation.

Industry analysts say many pharmaceutical and biopharma companies are turning their focus away from R&D and innovation, yet a recent survey by Quintiles and the Economist Intelligence Unit reveals that innovation is key to bringing new, more effective products to market to treat diseases.

The research also reports that while no single model works for all companies, the top innovators, those companies that are open to insights from many different sources, generated almost twice as many products and NMEs as their peers in the last three years.

The survey identified several barriers that prevent pharmaceutical companies from achieving or even pursuing innovation on a clinical front, including culture, which was identified as the primary obstacle. Culture was followed by high costs, complex regulations, and long development time scales.

Dr. Terri Cooper, principal at Deloitte Consulting LLP, and national leader of the life-sciences R&D practice, agrees that many companies often struggle with how to build innovation capabilities since the process encompasses a long-term strategy involving time and personnel resources as well as determination, with results measured in future value.

"Innovation can be at odds with, and sometimes overshadowed by, the immediate need to hit growth and profit targets," she says. "The need for different types of innovation is a factor as well — the radical, blockbuster big idea versus the more tactical, incremental and implementable idea, that yields smaller, but still valuable, results. In large companies, the search for the next big thing, such as a new pharmaceutical drug, technology, or device is often handled by creating a separate business unit devoted to the effort. But to generate smaller innovations, such as process or product improvements, or for smaller organizations without separate innovation functions, the goal is to cultivate and harness the ideas of the collective employee group."

Fostering Innovation

Deloitte researchers suggest that a number of strategic levers influence organizational culture, and these can be oriented in a way that fosters innovation. Some things to consider:

- **Leadership:** Incorporate innovation-focused competencies into the leadership profiles and emphasize the role of the leader to drive and support innovation at all levels of the organization.
- **Processes and Technology:** Formalize processes to allow employees to solicit, share, develop, prioritize, evaluate, and monitor new ideas.
- **Capabilities:** Define competencies and behaviors that support innovation, and incorporate innovation recognition into the goals, metrics, and rewards processes.
- **Structure:** Ensure organizational structures enable collaboration, and design roles and responsibilities of executives, managers, and staff to include opportunities to discover, incubate, and accelerate innovation.

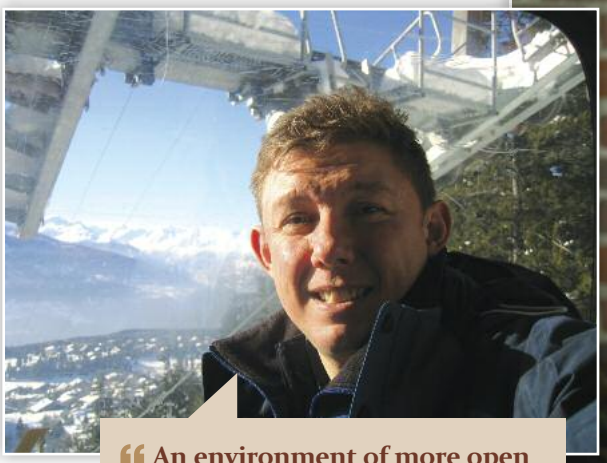
Source: Dr. Terri Cooper, Principal, Deloitte Consulting LLP, National Leader, Life Sciences R&D Practice.
For more information, visit deloitte.com.

> "Information systems, in particular, will need to change radically to provide fast, easy, and secure access to data for colleagues and partners alike."
>
> **JEN GOLDSMITH** / Veeva Vault

Innovation Through Partnerships

Several industry experts have identified the area around partnerships as being essential to increase innovation and create new opportunities.

Open innovation requires a flexible model where transformation comes from both internal



> **"An environment of more open scientific collaboration will provide increased focus around development, rather than a reinvention of the wheel."**
>
> **JOHN BLAKELEY** / ERT

> **"Incentives for the R&D organization should be aligned with company value creation, which is determined by successful product launches and a differentiated pipeline."**
>
> **DR. OLIVER FETZER** / Cerulean Pharma

and external ideas and where intellectual property is shared as a way to create value. While a relatively new concept in pharmaceutical drug development, open-source collaboration first began in the computer software industry.

Experts say the benefits of open innovation for drug development include access to knowledge and high-quality and reliable networks of strategic partners who can bring talented individuals to the table.

"Every company is concerned about its intellectual property and downstream profits," says John Blakeley, executive VP and chief commercial officer, ERT. "But an environment of open scientific collaboration can provide more focus around development rather than a reinvention of the wheel and speed success. The challenge of course is to work out how the downstream revenue can be managed in the appropriate manner."

Subhro Mallik, associate VP with the life-sciences practice at Infosys Ltd., says pharmaceutical companies have spent billions of dollars in internal R&D investment, and yet there are very few that have been able to capitalize on their investment; therefore some companies may be willing to adopt open partnerships as a long-term strategy and be willing to take the risk.

"On the other hand, there may be a movement during which pharmaceutical and biopharma companies break up their internal research organizations into smaller, nimble teams," he says.

Dr. Cooper says by moving to an open innovation model, Procter & Gamble now sources more than 50% of its new ideas from outside the company.

"There is no reason that this strategy cannot work for life-sciences companies," she says. "By engaging in open partnerships, companies can find new sources for intellectual property and source highly specific capabilities to develop their pipelines. Life-sciences companies — especially those looking to accelerate innovation without having to make significant new investments in R&D infrastructure — are finally starting to seriously look into developing ways to better collaborate with both traditional partners, such as CROs and academic research centers, and nontraditional partners, such as crowd-sourcing forums and users of their proprietary innovation portals."

Kiran Meekings, Ph.D., a consultant in the life-sciences consulting team at Thomson Reuters, says through the sharing of knowledge, resources, or experience, novel methods of collaboration can increase innovation, accelerate the drug discovery process, and capture new growth opportunities.

"Alliances with academic institutions can aid with target validation, high-throughput screening, and the identification of repurposing opportunities," she says. "Recent academic collaborative initiatives by GlaxoSmithKline, Lilly, Pfizer, and Bayer are already starting to produce positive leads."

The most recent company to pursue open innovation is Lilly, which in September announced the launch of a new open innovation platform designed to help build the company's pipeline and identify molecules that may have application for treating multidrug-resistant tuberculosis (MDR-TB).

The new platform, titled Open Innovation Drug Discovery, is supported by a new website available at openinnovation.lilly.com.

The program builds on the success of Lilly's Phenotypic Drug Discovery Initiative (PD2), which was launched in 2009 to facilitate research on molecules around the world that have the potential to ultimately be developed into medicines.

Improving innovation is essential for future success, but Robert Nauman, principal of Bio-

Pharma Advisors, says the investment by the life-sciences industry in this area is not being made.

"Pharmaceutical companies are not engaging so much in an open innovation model, as picking the right development horse that they hope will win the big race," he says. "We believe that in the not-too-distant future the cost to bring a fully developed product to market will be more than $1 billion."

Mr. Nauman says this may mean that a lot of good compounds may never see the light of day because they may only generate $250 million in revenue and cannot justify the research and development costs.

SOUND BITES FROM THE FIELD

The Top Trends Impacting R&D

JOHN ARROWSMITH, PH.D., is Science Director, Thomson Reuters, a source of intelligent information for businesses and professionals. For more information, visit thomsonreuters.com.

1. Regulatory hurdles on safety continue to rise, and for chronic treatments the thought of having to do multi-year morbidity and mortality studies can dissuade companies from investing in some disease areas.
2. Having sufficient differentiated drugs ready to emerge from the R&D pipeline in order to offset the patent cliff is a challenge, particularly in cancer and CNS. Differentiation is linked to personalized medicine and the challenges of lining up the right patient with the right drug occupy the minds of R&D leaders.
3. In the early pipeline, PoC (proof of concept) is still proving to be very challenging when the R&D hurdle is best-in-class or first-in-class; this applies to large and small molecules. Differentiation trumps novelty of mechanism.

BILL COONEY is President and CEO of MedPoint Communications Digital Inc., which provides specialized digital services to the global biopharma industry. For more information, visit medpt.com.

1. Finance: There is an immediate need to control costs of drug development. Runaway costs are unsustainable and reaching a tipping point.
2. Deconstruction: Biopharma companies will continue to outsource key functions, with clinical operations increasingly contracted out to more efficient providers on a strategic scale. Drug innovation will occur at small firms that are better suited for the high science of risk taking.
3. Globalization: Emerging countries will continue their ascent, both as markets for manufacturing and sales, and as regions for clinical research. The boom in clinical trials in emerging countries has slackened as industry has encountered many nuanced challenges, but this pause will only be temporary, as drug developers will overcome the learning curve when operating in different cultures.

FRANCES L. DEGRAZIO is VP, Marketing and Strategic Business Development, West Pharmaceutical Services, a provider of solutions for injectable drug administration. For more information, visit westpharma.com.

1. There is a need for industry to consider regulatory and insurance reimbursement requirements early in the development process.
2. There is a need to develop "new" products, rather than developing products where an equivalent brand already meets the market need. Such me-too products have only a small incremental value.
3. It is important to meet regulatory, compliance, and quality challenges early in development, particularly with regard to suitability of packaging. Early partnerships with packaging manufacturers can help to establish suitability and meet quality challenges throughout the product's life cycle.

DENISE (DEEDEE) DEMAN is Founder, Chairman, and CEO of Bench International, a global, executive recruiting and consulting firm serving the life-sciences industry. For more information, visit benchinternational.com.

1. Life-sciences companies are trending away from internal discovery stage investment, in favor of depending on the smaller, emerging companies to take the risk, in a form of "off balance sheet R&D."
2. At the end of the day, we will see thinner pipelines and significant pent-up demand for the return of scientific exploration on a broader scale. The smaller companies simply do not have enough to feed the demand.
3. There will be a deceleration in "R" and an increased dependence on "D," which will require companies to play catch-up for decades to come, if the life-sciences sector is to remain the architect of innovative discovery.

GLEN DEVRIES is President of Medidata Solutions Worldwide, a global provider of SaaS-based clinical development solutions that enhance the efficiency of customers' clinical trials. For more information, visit mdsol.com.

1. Productivity, as defined by an organization's ability to produce evidence in support of labeling claims, will emerge as the highest-level key performance indicator for any life-sciences company.
2. The most successful companies will start using more modern techniques, including automation, more dynamic processes, and quality-enhancing risk-based approaches to run clinical trials at a lower overall price point per study.
3. Competitive dynamics between CROs competing for more prevalent outsourcing, as well as internal sponsor teams looking to differentiate their contributions to the development life cycle, will create an environment where process change and continuous improvement will become the norm, instead of a rare exception.

DAVID FISHMAN is President of Snowfish LLC, a marketing firm focused on the pharmaceutical, biotechnology, and medical device industries. For more information, visit snowfish.net.

1. Given the advances in genomics, the age of personalized medicine is fast approaching. Studies today that are not now set up based on genetic profile, will be in the future.
2. The increasing failure rate of Phase II and III products is forcing companies to look outside their traditional product development pipelines.
3. Mergers and acquisitions are having a greater importance in filling product pipelines.

SEAN MCCARTHY, D.PHIL., is CEO of CytomX

Challenges of Open Innovation

Dr. Cooper says the hurdles to open innovation are largely the same as for other forms of collaboration in that strong leadership, clear governance processes, information security, and enabling technologies are needed to be successful.

"These challenges are magnified, however, by the sharing of intellectual property," she says. "Pharmaceutical companies considering open innovation will need to make sure they have the proper agreements, standards, and committees in place to manage these collaborations and ensure they are adding value to

Therapeutics Inc., a privately held biotechnology company developing Probodies, or proteolytically activated antibodies. For more information, visit cytomx.com.

1. Reclassification of disease and tailored therapy: As molecular techniques, including next-generation sequencing and proteomic analysis, become more widely available, the molecular dissection of disease will continue to result in more efficient targeting of therapies to the places they will work best. Advances such as these mean that diseases that are pooled together today under outdated diagnostic classification systems, and therefore treated as single conditions, will be re-classified and their treatment will become dramatically more effective.
2. A drive to more efficient operating models: Small groups have shown the ability to consistently outperform in metrics such as IND filings per year. The reasons for this are social (e.g. close teamwork), motivational (e.g. employee ownership), and practical (e.g. co-location). As such, pharma will continue to experiment with biotech organizational models in an attempt to capture these efficiencies enjoyed by smaller biotech companies.
3. Targeting of biologics: With tens of antibodies, cytokines, and hormone therapies already FDA approved and several hundred in development, the golden age of biologics is upon us. But these classes of drugs are not immune to dose-limiting toxicities that either prohibit their fully effective clinical use or render their successful development impractical at best, and impossible at worst. Various targeting approaches are being developed, including antibody-drug conjugates, bi-specific antibody formats, and pro-biologics that become selectively activated at sites of disease.

STUART W. PELTZ, PH.D., is President and CEO, PTC Therapeutics Inc., a biopharmaceutical company focused on the discovery, development, and commercialization of orally administered small-molecule drugs that target post-transcriptional control processes. For more information, visit ptcbio.com.

1. In the United States, the implications of national healthcare reform and the overall healthcare spend will be an important influence and will shape R&D budgets, priorities, and strategies moving forward.
2. The degree to which the government continues to fund the NIH and other agencies that fund basic and applied research as well as clinical trials. Reductions in funding will impact innovation and reduce the nation's competitiveness in areas where we are currently a world leader.
3. Upcoming patent expirations on blockbuster drugs will continue to affect how companies prioritize R&D and build their pipeline — both from within and through partnerships and acquisitions. The growing market opportunity in BRIC nations will provide a source of revenue growth, which could offset the pending patent cliff.

JOHN ROTHMAN, PH.D., is Executive VP, Science and Operations, at Advaxis Inc., a biotechnology company developing the next generation of immunotherapies for cancer and infectious diseases. For more information, visit advaxis.com.

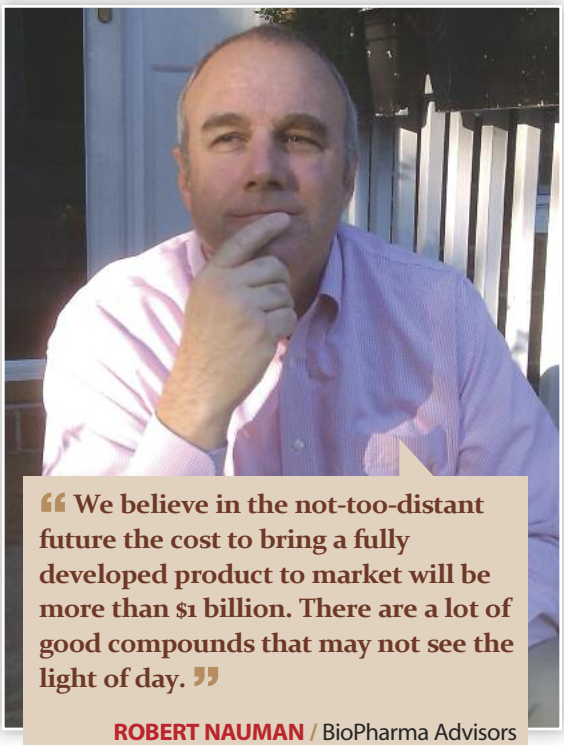
1. The ability to use living bioengineered organisms as drugs is an opportunity to create new classes of therapeutic agents that may have greater safety and efficacy than current treatment modalities. For example, by using pathogens that have evolved to infect us, and to which we have evolved immune mechanisms to thwart infection, these agents enable us to access hardwired evolutionary immune mechanisms that we are born with to fight that specific pathogen, and redirect these responses to those Pathogen Associated Molecular Pattern or Danger Associated Molecular Patterns to cancer or other infectious disease. The immune response to living, metabolically and reproductively competent, bacteria is considerably more complex than the response to synthetic chemicals or antibodies, and enables stimulation of diverse and integrated mechanisms not previously possible.

KK RUMRILL is Client Services Director at BBK Worldwide, a provider of patient recruitment services for clinical trials. For more information, visit bbkworldwide.com.

1. Social media will be an ever-evolving component of patient recruitment for the foreseeable future. But with as many potential pitfalls as opportunities, it is vital for sponsors to stay informed and proceed, however cautiously, with an online strategy for connecting with patient audiences.
2. Patients will share their opinions, including negative clinical trial experiences, and may even comment on adverse drug events in online forums whether you join them in the online environment or not. Before long, sponsors will not have a choice whether to participate in social media. Only decisions about how, when, and where to incorporate online programs will remain.

LEE VALENTA is President of OptumInsight Life Sciences, which specializes in technology, information, analytics, business, and consulting services. For more information, visit optum.com.

1. Many life-sciences companies need to alter how they develop their pipelines to leverage all the data and tools available to help them. This will enable a better review and understanding of what is needed to maximize chances for regulatory, reimbursement, and marketing success.
2. By using evidence mapping, based on proven real-world evidence and data-based analyses and projections, products and protocols would be developed in a way that will resonate with regulators and payers.
3. Looking at compounds based on the value they'll need to deliver enables companies to make smarter pipeline decisions earlier, getting ahead of more complex risk-benefit calculations.



> **"We believe in the not-too-distant future the cost to bring a fully developed product to market will be more than $1 billion. There are a lot of good compounds that may not see the light of day."**
>
> **ROBERT NAUMAN** / BioPharma Advisors

> **"Collaboration and information sharing are key to any strong partnership, but companies need to ensure that its IP position is well-protected before entering into any new partner relationship."**
>
> **DAVID WOLF** / Hamilton Thorne

their organizations. In addition, the engagement between partners will need to happen at the senior level to make sure both parties are providing value to the program and achieving their goals through the collaboration."

Elliott Berger, VP, global marketing and strategy, at Catalent, says a collaboration model requires a new degree of flexibility in both R&D operations and legal terms to be able to cooperatively develop new products, manage IP issues, and accelerate speed to market.

"The traditional 'all expertise inside the wall' models that worked so well previously need significant adjustments both in terms of mindset and process," he says.

Oliver Fetzer, Ph.D., president and CEO at Cerulean Pharma, agrees, stating that overcoming established large pharma traditions and ways of doing business is the biggest challenge.

"Companies need to change their mindsets, attitudes, goals, decision-making capabilities, and incentive structures if they are to engage in open innovation," he says. "Clearly, this is not an easy transition. But it is encouraging to see that several large pharmaceutical companies are now openly acknowledging the need for this type of change and some are taking serious steps to make it happen."

Dr. Fetzer says those at the top of an organization have to properly define innovation so that it is more than a buzzword.

"Innovation has to be grounded in a clear mission that is 'lived' in the way decisions are made," he says. "Incentives for the R&D organization should be aligned with a company's value creation, which is determined by successful product launches and a differentiated pipeline. An aligned incentive structure based on long-term value creation through innovation will serve companies far better than focusing too much on short-term candidate advancement goals."

Neil MacAllister, chief business officer at INC Research and president of AVOS Consulting, says, however, there is a dynamic happening at the basic research level that is complicating open innovation.

"The drug industry is moving away from discovery in a big way; companies have cut scientific headcount and R&D budgets," he says. "At the same time, more federal grants for academic research are requiring commercial endpoints. Academic institutions are under pressure to convert grants to patents with commercial propositions before handing them over to the drug industry. To some degree, the tightening of basic research dollars is compromising the open innovation model. In response, academic industry collaboration is becoming more pronounced than ever before."

Mr. MacAllister says the biggest issue with academic industry collaborations is the cultural divide between academia's thirst for knowledge and a drug company's thirst for commercial products.

"They do not speak the same language when discussing preclinical and clinical processes," he says. "CROs are able to fill this gap and provide a translational function between institutions and drug developers as they understand and can articulate both the science and operational know-how; something they do as a normal course of business."

Partners in Innovation

Strategic partnerships are key to competitive advantage in the new model of open innovation, says Nagaraja Srivatsan, senior VP and head of life-sciences, North America, for Cognizant.

"Governance at all levels ensures the correct level of involvement of both executive and operational leaders, and by tracking and monitoring appropriate metrics, pharmaceutical companies can leverage a balanced scorecard that will ensure the realization of common goals of the partnership," he says.

Kimberly Ramko, Americas life-sciences sector leader for advisory services, at Ernst & Young, says pharmaceutical companies that are willing to collaborate externally with partners such as other pharma, biopharma, or medical device companies, as well as academic medical centers, payers, and providers will benefit from a reduced time to market while sharing the risk and reward.

"Creating collaborative business models around a specific disease state with these partners as well as technology-based partners, such as wireless device companies, social media, and managed service providers, will enable life-sciences organizations to have more control of their product perception in the market, while also gaining more meaningful insights and opening up new avenues of market access," she says.

David Wolf, CEO of Hamilton Thorne, says for companies to truly collaborate, there needs to be more information sharing between partners on not just the perceived advantages of the alliance, but also the potential or current technical hurdles that need to be

addressed throughout the development cycle.

"With a model of a more open partnership, both companies can speed up the development process and prevent fewer issues, while still protecting their IP position," he says. "Collaboration and information sharing are key to any strong partnership, but companies need to ensure that their IP position is well-protected before entering into any new partner relationship."

Jen Goldsmith, VP at Veeva Vault, agrees that an open innovation model requires information sharing across companies and around the globe.

"Incremental change is no longer enough," she says. "Information systems, in particular, will need to change radically to provide fast, easy, and secure access to colleagues and partners alike. At the same time, application complexity must be reduced so that training for partners and vendors is a matter of minutes not hours or days.

> **"Academic institutions are under pressure to convert grants to patents with commercial propositions before handing them over to the drug industry."**
>
> **NEIL MACALLISTER** / INC Research

"For years, life-sciences organizations have been generating data and documents across the business in support of specific research, development and other activities," Ms. Goldsmith continues. "In many cases, this information was created, used, and archived in a way that made it inaccessible for future endeavors. Today, new information technologies make it easier than ever to unlock the potential of these underused information assets, a process that will prove critical to future innovation." PV

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Denise Myshko

ENSURING Pipeline Growth

Pharmaceutical companies must develop strategies to enhance the drug development pipeline to ensure future success.

> "In the next five years, companies have to create more business applications in the areas of simulation and modeling; integrate genomic data and information across all phases of clinical development; and understand and leverage patient-centric information in all aspects of clinical development."
>
> **NAGARAJA SRIVATSAN** / Cognizant

The 2011 edition of the Pharmaceutical R&D Factbook reports that R&D expenditures continued to drop in 2010 to an estimated three-year low of $68 billion, which is in stark contrast to the growth rate leading up to 2008.

The report, complied by CMR International, a Thomson Reuters business, also highlights that drug success rates continue to show the declining trends of the past decade. There were 55 Phase III drug terminations during the 2008 to 2010 time period, more than double the number of terminations from 2005 to 2007; in addition the number of drugs entering Phase III clinical trials fell by 55% in 2010.

"R&D productivity — the probability of success — is declining, and more products are failing in late-stage clinical development," says Dr. Terri Cooper, principal, Deloitte Consulting LLP, and national leader, life-sciences R&D practice. "The complexity of new products demands more efficient patient and investigator targeting, more efficient clinical operations, and the right choice of geography. An inflexible R&D sector creates overcapacity, which allows sub-standard products to progress, and under-capacity, which limits investment in promising compounds."

Dr. Cooper says current biopharma R&D operating models lack the flexibility required to effectively apply the research capacity to meet shifting demand.

"As a result, R&D is plagued by operational and governance constraints that drive up costs and limit choices at key stage gates, creating a variable and unsustainable flow of low-value products through the pipeline," she says. "To rebuild sustainable pipelines with high-value products, R&D organizations must focus on actively balancing resources across the pipeline to consistently align capacity with demand and create choices that will

differentiate products. In many organizations this will require wholesale operational, structural, and cultural transformation. We believe this change needs to occur now, as other options such as M&A, licensing, outsourcing, and cost-cutting alone cannot support long-term growth."

Past attempts by large pharmaceutical companies to improve discovery and development productivity by setting numerical goals for candidate advancement to the next stage led to unintended consequences, says Oliver Fetzer, Ph.D., president and CEO, Cerulean Pharma.

"Advancing candidates frequently did not translate into more successful product launches as late-stage development failures in Phase III or during regulatory review have increased," Dr. Fetzer says. "It is extremely important to impart a holistic drug development mindset in the R&D organization that is distinct from focusing on candidate advancement. The organization needs to define what innovation is needed, translate that into product profiles, and ensure that each part of the organization understands what part it plays in meeting or exceeding the product profiles."

Life-sciences companies have deployed a number of strategies to address falling productivity, but these strategies have resulted in limited success, Dr. Cooper says.

"High-performing R&D organizations across the industry differ in size and structure, but share key operational attributes and strategies," she says. "At the core, they focus on flexibility, balancing demand and supply, generating choice, and maintaining a sustainable pipeline flow."

Dr. Cooper says by working with these organizations Deloitte has been able to dig a little deeper, and has found that these companies' operating models achieve the following: demand and attrition are accurately defined and understood, and operating targets are developed based on clear metrics; resource allocation creates balanced and flexible supply to support efficient asset utilization; capacity supports the work required to consistently meet operating targets and creates a sustainable pipeline flow; and choice is created across the pipeline so that the most promising products progress and create value.

Dr. Fetzer says many of the traditional partnership and collaboration models are being revisited to achieve greater innovation and productivity.

"In the end, it comes down to harnessing what each partner is really good at," he says. "Those partnerships that can build on a biotech's functional integration, nimbleness, sense of urgency, and focus to discover and develop innovative molecules and marry them to the resources, global expertise in regulatory and commercialization of large pharmaceutical companies will be at an advantage over traditional fully integrated models."

FAST FACT

ONLY 21% OF RESPONDENTS IN A RECENT SURVEY WERE HIGHLY CONFIDENT IN THE ACCURACY OF THEIR STUDY BUDGETS, WHILE ALMOST HALF OF RESPONDENTS REPORTED VARIANCES OF 11% OR GREATER FROM FORECAST TO ACTUAL STUDY COSTS.

Source: ClearTrial

Clinical Trial Facts

The pharmaceutical industry spent less on drug R&D last year than at any time in the last three years, according to data released from the 2011 Pharmaceutical R&D Factbook complied by CMR International, a Thomson Reuters business.

Key highlights:

- 21 new molecular entities (NMEs) were launched on the global market in 2010, a decrease from 26 in the previous year.
- 2010 saw the lowest number of NMEs launched by major pharma in the past 10 years.
- The number of drugs entering Phase I and Phase II trials fell 47% and 53% respectively
- Self-originated molecules have a 20% greater chance of reaching the market from Phase III and submission versus in-licensed or acquired compounds.
- Patient recruitment for clinical trials has shifted towards Southeast Asia.
- The proportion of total sales from drugs reached an all-time high of $856 billion, according to IMS Health.

Source: Thomson Reuters. For more information, visit cmr.thomsonreuters.com/services/factbook.

Pipeline Best Practices

According to Charles Bramlage, president and CEO of Pearl Therapeutics, there are three keys to ensuring pipeline growth and productivity: focus on establishing a diversified balanced pipeline; recruit and retain highly motivated talent; and foster a zeal for innovation at all levels: scientific, operational, and business arrangements.

"In addition, over the next five years, as pharmaceutical companies struggle with patent cliffs, reimbursement issues, healthcare reforms, and a nonsupportive political landscape, adequate funding will be a priority in any company's R&D efforts, regardless of business development goals," he says.

Neil de Crescenzo, senior VP and general manager at Oracle Health Sciences Global Business Unit, says to shift the odds toward pipeline growth and improved R&D productivity, organizations require early and accurate insight into which candidates are most promising.

"They require expanded visibility into their clinical trials at the individual, group, and enterprise level," he says. "Expanded insight into the trial portfolio enables organizations to more closely monitor and manage individual trials and portfolios to identify potential issues early. This approach also enables synergies and efficiencies that might not have been identified in a siloed trial management environment."

David Wolf, CEO of Hamilton Thorne, says companies need to take a critical look at their pipelines and assess where the real opportunities are, and not what can easily be developed.

"Building off of internal technology assets is certainly the main driver of most R&D or-

FDA Commissioner Outlines Steps to Spur Biomedical Innovation

In October, FDA Commissioner Margaret Hamburg, M.D., released a blueprint containing immediate steps that can be taken to drive biomedical innovation, while improving the health of Americans.

Titled "Driving Biomedical Innovation: Initiatives for Improving Products for Patients," the document addresses concerns about the sustainability of the medical product development pipeline, which is slowing down despite record investments in research and development.

"America is at an important crossroads, where the science before us presents unprecedented opportunities to create new and better medical products and to promote better health for the public," Dr. Hamburg says. "Our innovation blueprint highlights some of the initiatives the FDA will be implementing to ensure that these opportunities are translated into safe and effective treatments that can help keep both American patients and American industry healthy and strong."

While the FDA has long been committed to promoting innovation, and with a number of efforts under way already this year, Dr. Hamburg recognized the need to create an FDA-wide framework to address the changing scientific landscape. This blueprint launches the Innovation Initiative, identifying additional steps the agency can take immediately to address the most pressing concerns facing patients and industry.

The blueprint focuses on implementing the following major actions:

- Rebuilding the FDA's small business outreach services
- Building the infrastructure to drive and support personalized medicine
- Creating a rapid drug development pathway for important targeted therapies
- Harnessing the potential of data mining and information sharing while protecting patient privacy
- Improving consistency and clarity in the medical device review process
- Training the next generation of innovators
- Streamlining and reforming FDA regulations

Source: U.S. Food and Drug Administration.
For more information, visit fda.gov.

Dr. Margaret Hamburg

ganizations, but new partnering and distribution opportunities, especially in new and emerging markets, will also be key to a pharmaceutical company's pipeline health," he says. "Finding the market gaps, based on proven market research and a solid distribution channel, will ensure that the product pipeline not only can be filled but also successfully sold."

Kiran Meekings, Ph.D., consultant in the life-sciences consulting team at Thomson Reuters, says strategies being used by pharmaceutical companies to enhance pipeline value include pursuing orphan and rare disease targeting, portfolio management strategies, patient stratification strategies, repurposing and risk sharing arrangements, or financing deals.

"These development strategies have the potential to reduce development times, costs, or risk while maximizing an asset's revenue potential," she says.

Dr. Meekings also says pharmaceutical executives are investing in repurposing strategies, both within their organizations and via industry-wide initiatives, as a way to maximize the value of their company's existing assets.

"Success rates for repurposed drugs are higher and costs are lower than de novo R&D," she says. "It is estimated that about 2,000 drugs have passed stringent early-stage safety tests but have failed from lack of efficacy in Phase II/III clinical trials. This number grows at the rate of 150 to 200 drugs per annum. The life-sciences industry is looking to this pool of drugs with attractive R&D metrics to replenish the diminished pipeline and address falling productivity."

Mr. de Crescenzo says more specialized research groups are focusing on targeted disease areas to develop drugs for smaller market populations and address unmet medical needs.

"This movement is being facilitated by advances in genomics and proteomics, as well as IT technology," he says. "But emphasizing specific disease areas with smaller patient populations also means reduced market potential, and, regardless of the size of the patient population, the cost of bringing a drug to market remains about equal. Organiza-

Strategies to Address Falling Pipeline Productivity

1. **Implement concept trials** to fill the pipeline with promising drug candidates. A concept trial is not designed to establish the efficacy of a particular candidate, but rather to help researchers decide if the candidate is worth testing in larger Phase III trials. Concept trials are effectively being implemented for vaccines and can be extended to other drugs as well.
2. **Leverage new technologies** to reduce the cost and improve the approval success rate of the drug. Pharmaceutical companies should look to use more in-silico diagnostics, simulation, and modeling to clearly determine the benefits of the drug candidates early in the drug life cycle, improving the overall R&D throughput.
3. **Incorporate the comparative effectiveness approach** early in the process to ensure that the right types of trials are being advanced.
4. **Leverage patient-reported outcomes** early on the drug development process to ensure better outcomes by incorporating real patient feedback on the product.
5. **Integrate drug safety teams early in the drug development process** to provide better context to the safety and efficacy of the product. Having the pharmacovigilance teams participate in clinical trial design will ensure that the right types of products are advanced and prevent expending effort on clinical trials that have a low probability of success, especially from a safety perspective.

Source: Nagaraja Srivatsan, Senior VP and Head of Life-Sciences, North America, for Cognizant.
For more information, visit cognizant.com.

tions, therefore, need to not only increase capacity, but R&D efficiency, as well, to ensure that adequate resources can be deployed to move promising candidates through the development process.

"Without clinical data that are well-organized, easily accessible, and thoroughly documented, the value of a drug may not be fully realized until late in the development cycle when the decision to terminate a candidate is most expensive," Mr. de Crescenzo continues.

Increasingly, R&D productivity will be influenced by the quality of the technology and tools used to run clinical trials, and the care with which data are collected and analyzed, agrees Adam Butler, VP, client services, Bracket.

"A reinvestment in technology tools to improve R&D productivity represents a tremendous opportunity for companies to improve both the efficiency and outcomes of clinical trials," he says.

Mr. Butler adds that the continuing expansion of Phase II and III clinical trials into emerging markets and across the globe is shifting R&D best practices.

"Patient recruitment, GCP, and adaptation of endpoints have all introduced new complexities to clinical studies that require a greater investment of time and money to ensure quality programs," he says.

Sanjeev Wadhwa, principal, life-sciences advisory services at Ernst & Young, says the future of networked R&D is in virtual biotechs that leverage biological networks that integrate diverse data sets, including electronic healthcare information, and established disease models. These open-access, integrative bio-networks will involve a coalition of partners trying new methods of drug discovery and evolve with the contributions of many scientists in a distributed framework that will build disease models.

"Disease network models integrating translational research and individual patient care pathways are creating an innovative paradigm shift in various business models," he says. "These quantitative disease models built on collaborative public-private partnerships will usher a radical transformation of product-centric pharma IP portfolios into a truly visionary and universally 'humane' platform with the greatest potential of uncovering pre-symptomatic patient populations which will benefit from new therapies. They represent a spectacular opportunity for pharmaceutical companies to create entirely new patient-centric markets driven by new therapeutic insights and accelerated scientific discoveries built on preventative, predictive healthcare evidence-base while improving care delivery in specific diseases."

Nagaraja Srivatsan, senior VP and head of life-sciences, North America, for Cognizant, says in the next year, companies need to clearly understand core and non-core activities and outsource non-core capabilities; develop a better decision infrastructure, such as data repositories and dashboards to bring together historic and current clinical trial information; create a collaborative environment with internal and external partners to ensure consistent business outcomes; incorporate drug safety and PV teams early on in the drug development process; and have an approach to clearly articulate comparative effectiveness early in the clinical trial process.

"In the next five years, companies have to create more business applications in the areas of simulation and modeling; integrate genomic data and information across all phases of clinical development; and understand and leverage patient-centric information in all aspects of clinical development," Mr. Srivatsan says. PV

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