BY TAREN GROM

A Long and Winding ROAD

By addressing failing R&D models, collaboration issues, complex global trials, development bottlenecks, and a changing regulatory landscape, sponsors and their partner companies can improve development efficiency.

In today's biopharma economy, declining R&D productivity combined with increased development costs have made investment portfolio managers skittish, says Chip Gillooly, VP, capital, at Quintiles.

"The risks associated with investments are high, and the lack of output is making everyone nervous," he says. "To manage this new high-risk environment, and continue to deliver valuable and accessible therapies, biopharma companies must find ways to increase output, decrease costs, and eliminate unnecessary layers of bureaucracy that hinder productivity. As new drug applications arising from discovery efforts have dried up, investors and executives have relied on M&A activity to fill their pipelines, enhance their portfolios, and gain access to new products."

A New Model

Biopharma companies will continue to pursue these opportunities, Mr. Gillooly says, as a means to shore up business and reduce costs, but they are short-term solutions that do not position companies to sustain their business.

"Quite simply, companies cannot cut their way to either success or long-term profitability," he says. "The availability of acquisition and in-licensing opportunities cannot — and should not — impede the drive for innovation. Forward-thinking companies are expanding into complementary markets, including biosimilars, diagnostics, and over-the-counter medicines, to create a more diverse portfolio that will better address global healthcare needs."

James DeSanti, founder and CEO of PharmaVigilant, believes R&D organizations are banking on technology as a means to restructure and innovate.

"This means technology vendors will have to become more flexible with their tools and solutions to better adapt to this new breed of R&D," he says. "There is still so much to be discovered and improved upon in terms of clinical trial technology, and so many of the current vendors are just scratching the surface. In the future, I expect technology to take R&D in a new direction, creating an agile and streamlined model that ensures new medicines are brought to market faster than ever before."

Nagaraja Srivatsan, VP and head of life sciences, North America, Cognizant, believes the next-generation R&D model will be driven by several trends.

"Strategic alliances and new technologies are expected to fuel growth," he says. "With the aid of new technologies, targeted medicines will become future drivers of the market. Drugs that target niche markets will have less competition and, hence, will serve to address various unmet needs of the population. Pharmaceutical organizations are slowly shifting from the blockbuster model in light of this emerging trend."

The development and management of innovation networks will create a variety of strategic partnerships, academic collaborations, and outsourcing opportunities that will enable pharmaceutical companies to reduce development times and improve productivity of the R&D process, Mr. Srivatsan says.

"Life-sciences companies will develop 'externalization platforms' and associated governance processes to manage the external partnerships comprehensively in a seamless manner," he continues. "They will also leverage offshoring and outsourcing to focus on core competencies such as new therapeutic areas, global trials, or technology development while partnering with a core set of service providers having broad and deep domain capabilities in obtaining data/information-intensive services globally at lower costs."

Mr. Gillooly agrees that sponsors are likely to adopt a more comprehensive outsourcing strategy to enhance productivity.

"By outsourcing functions such as data management, biostatistics, sales, medical education, and safety monitoring, biopharma companies can minimize their own permanent infrastructure needs and focus on their core strengths, with the confidence that well-chosen partners can aptly manage non-core activities," he says.

Kevin Hrusovsky, president and CEO of Caliper Life Sciences, says while the 21st century has witnessed great strides in the life-sciences research tools industry, it has also witnessed a concomitant decline in productivity in the pharmaceutical industry, to the extent that small-molecule R&D is often a loss-making exercise.

"Furthermore, despite the decline in new drug approvals over the past decade, the cost of pharmaceutical R&D has continued to climb," he says. "The problem of declining ROI is exacerbated by erosion of the generics market, increased scrutiny from the FDA on the issue of drug safety, price controls and pressure from pending healthcare reform legislation, and increased hurdles for safety and/or efficacy in the new era of comparative effectiveness, which essentially requires new drugs to be differentiated from those already on the market."

NAGARAJA SRIVATSAN ■ *Cognizant*

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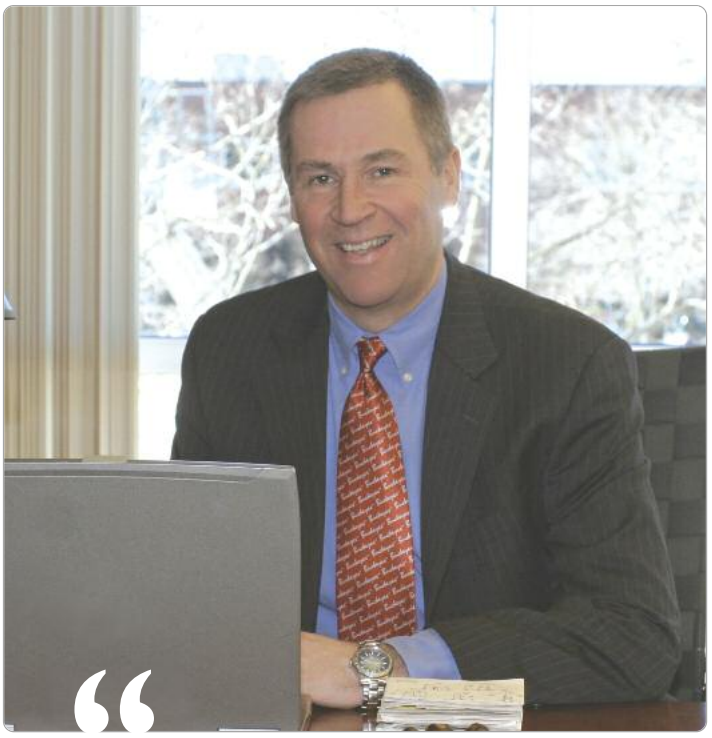
Mr. DeSanti says two of the biggest challenges in R&D are speed and resources — both are in high demand, but can be scarce among even the largest biopharmaceutical companies.

"Any resource that is not considered essential to the discovery and development process is being cut — this certainly helps to curb costs, but it can also cause delays," he says. "Companies must learn how to create an effective balance between these two opposing factors."

Working Together

Robin Winter-Sperry, M.D., president and CEO, Scientific Advantage, and Science Oriented Solutions (SOS), says ideally the R&D and commercial teams should begin working together in a graduated fashion starting in Phase I.

"One very effective model is to have a cross-functional project team that starts with clinical development chairing the team in early-phase development, then switching to a commercial lead once the agent moves into Phase III development," she says. "This approach provides cross-functional team input at all phases of



KEVIN HRUSOVSKY ■ *Caliper Life Sciences*

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development, the creation of valuable milestones, including go/no go criteria, and an integrated commercialization plan."

Darshan Kulkarni, Pharm.D, Esq., principal attorney, Kulkarni, agrees that the R&D and commercial teams should begin working together the moment there is a need to begin tempering science with practicality and assessing the marketability potential of a product.

"The current model of innovative drug development primarily includes two players: smaller pharmaceutical, biopharmaceutical, and medical-device companies that take the risk of early drug discovery; and larger players that take early to midstage products and bring them to market," he says. "These smaller innovator companies are often composed primarily of scientists who take on the risk of drug development. They then may license or sell the product and/or company to larger pharmaceutical players after a certain milestone of success has been achieved. In these smaller companies, commercial teams that can temper the scientific knowledge of the inventors with business acumen can better position the target product for appropriate licensing and/or sale opportunities. Larger pharmaceutical companies, at the point of in-licensing/purchase, often perform substantial due diligence on the target products and/or company to minimize the risk associated with the purchase of the license/ option/company. Commercial teams are therefore necessary on both sides to effect an appropriate sale. After the point of sale, commercial teams are necessary to position the product for maximized profitability. A successful partnership between the R&D and the commercial arms is important to bring a product successfully to market, since the commercial team can help bring practicality to the scientific process."

Fran DeGrazio, VP, marketing and strategic business development, at West Pharmaceutical Services, says by working closely together, the two teams can differentiate their product through the packaging and delivery systems.

"There are several reasons the relationship should start early," she says. "The first is to ensure that the packaging is right for the drug product. Packaging can be a major factor in the success of a drug product getting through the regulatory approval process smoothly and to the market quickly. R&D and product development should determine how the product is going to be delivered based on the clinical application. This will help them to understand what type of primary packaging is needed, and how that packaging will fit with the delivery system."

Going Global

With increasingly complex global studies, biopharmaceutical companies must access comprehensive, integrated information throughout clinical development.

"It is imperative to be able to gain greater visibility into trials and improve data access for better, faster decision-making," says Mark Goldberg, M.D., chief operating officer, Parexel International.

"New operational models, supported by technology, can help biopharmaceutical companies improve productivity, decrease costs, and run trials more efficiently, ultimately achieving greater benefits through faster execution," he says. "Standalone systems to facilitate trials are not well-integrated; therefore, the opportunity to maximally leverage technology is limited. This challenge is being addressed through more integrated e-clinical solutions that are interoperable and aligned to accelerate clinical development."

Despite the many advantages related to global trials, there is, however, some disagreement on the impact global trials have on drug development.

"Some believe that the ability of using patients from different countries may drop the cost of conducting clinical trials, since the cost of recruiting an individual patient may be lower," Dr. Kulkarni says. "Others counter that the cost of adding regulatory and management personnel to monitor the requirements in the various countries, and to coordinate global clinical trials, can nullify the cost savings of conducting trials globally. There is truth to both sides of the story. While a global clinical trial may be lower in costs in terms of patient recruitment, the cost of ensuring that requirements such as adhering to GCPs and other applicable regulations are met, as well as study coordination costs, and auditing costs may nullify those savings. There should therefore be compelling reasons, other than cost savings, to conduct global clinical trials. Such reasons may include wanting to test in diverse patient populations, evaluate safety and efficacy requirements for multiple countries, and finding treatment-naive patients."

Michael Parisi, president of Altum, part of CommonHealth, concurs, adding the very foundation of clinical trials represents everything positive that research is trying to accomplish: faster clinical trial accrual, results that deliver critical answers, and accelerating the next phase of studies to gain even greater insight into a disease and its treatment.

"From a societal perspective, well-designed and controlled global trials can help raise the local standards of care within a given geography by providing information and access to the latest technology and care," Mr. Parisi says. "We have seen huge strides in the prevention, screening, diagnosis, and treatment of HIV in all corners of the world, even in those geographies that are often neglected. These advancements would not be possible without the coordination and partnership between global health organizations, patient advocacy, philanthropy, and the pharmaceutical industry."

Mr. Gillooly cites another example where global trials are helping to push science forward.

"In cancer research alone, the time saved from globalization is extraordinary," he says. "If the 2,296 cancer agents currently in clinical research relied on U.S. patients alone as volunteers, it would take five years to complete Phase III trials. If the same research is conducted using a global population, the trials could be completed in two years, poten-

FRAN DEGRAZIO ■ *West Pharmaceutical Services*

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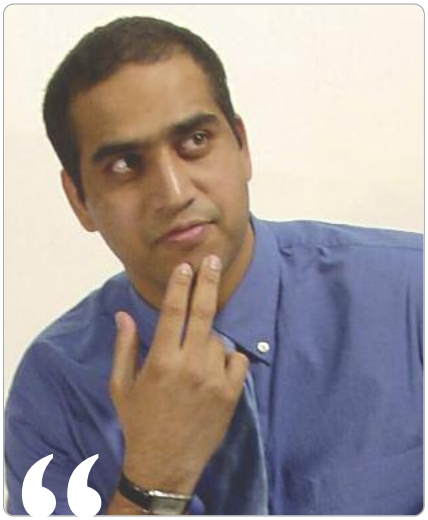

DR. DARSHAN KULKARNI ■ *Kulkarni*

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tially enabling the introduction of a new generation of cancer medicines in a fraction of the time. Globalization enables drug developers to cut years from trial times by using global patient pools, often in emerging regions where costs are lower."

Unclogging Bottlenecks

Michael Naimoli, U.S. life sciences industry solutions director, Microsoft, says one of the biggest challenges facing the industry today stems from the fact that during the development of new drugs, thousands of documents are created and must be tracked and managed.

"Time spent searching for documents or entering metadata manually can delay overall time to market," he says. "Being able to efficiently find and deliver product documentation internally and externally is essential for successful product development and streamlined business processes."

Exacerbating this challenge is the fact that the industry must increasingly consider the potential acquisitions available to them as part of the pipeline.

"While companies may not formally own these compounds for development, they must consider them as options for acquisition and inclusion in their drug development options," Mr. Naimoli says. "This acutely intensifies the need for content management beyond simply documents, to the secure exchange of data that represents key intellectual property."

Best Practices for Improving Efficiency

Scott Treiber, executive VP, clinical development solutions, inVentiv Clinical Solutions, says there are steps companies can take to ensure they are spending efficiently on clinical trials and not wasting limited resources.

"First, it is worthwhile to take extra time and effort to ensure that the trial is well-designed from the inception of the study," he says. "Poorly designed study questions can be costly in the long run and deliver more questions than answers. In addition, the following actions can assist in streamlining the clinical study process: allow the label to drive the study design; consider small-scale feasibility studies to assess population and efficacy endpoints at small costs. Later studies can be simplified based on information from pilot studies; keep it simple — simple studies have proven more likely to be on time and on budget; talk to the FDA early and as often as possible; and adhere to FDA recommendations unless there is a strong argument to counter their recommendations."

Mr. DeSanti says there are a lot of opportunities to improve relationships with sites during the development process, which can drastically improve R&D efficiency.

"Streamlining the monitoring process at the site level not only provides significant cost savings, but it also results in a decrease in disruptions," he says. "These efficiencies can be achieved through remote monitoring technology."

Mr. Hrusovsky provides a four-point strategy to successfully leverage technology for efficient R&D.

One, he says, life-sciences tools should be judiciously used to create more efficient and productive innovation cycles through rapid, cost-effective reiterative selection and optimization. Two, the clinical relevance of early-stage R&D must be enhanced by making the process and data more predictive of clinical outcome, essentially by creating an in vitro to in vivo bridge. Three, to ensure precise and immediate control over critical-path activities, each step of the integrated innovation cycle and in vitro to in vivo bridge must be evaluated to determine which activities should be kept under internal control by the drug developer. And four, early cumulative data should be leveraged to reiterate the process to develop new drug candidates with optimal safety, efficacy, and desirable attributes that will help differentiate the final products from a competitive standpoint.

"It is vital to include a continuous improvement feedback loop in early-stage drug development," Mr. Hrusovsky says. "Allowing the developer to reiterate where appropriate, and to reach a go/no go decision more quickly and with a higher level of confidence, will ultimately mean more efficient and cost-effective drug development and a higher likelihood of achieving positive ROI for a given candidate. To guarantee swift and efficient execution of the innovation cycle, it is important to maintain control of these critical activities in-house, contrary to the current trend of outsourcing, which often loses sight of the importance of maintaining control of strategically valuable activities."

Jens Oliver Funk, M.D., senior VP and global head of TA oncology at EMD Serono, says despite many attempts to increase R&D efficiency, the overall success rates to market a new drug candidate entering Phase I clinical development have not changed substantially over the past several years across the industry.

"It is key to be able to identify the winners early in the clinic, while terminating the others in time as soon as data allow," Dr. Funk says. "This notion of early data-driven decisions requires a rigorous orientation towards proof-of-concept (POC) trials with an intent to ask key questions with reference to drug proof-of-mechanism in humans, PK/PD relationships, and stratified patient subsets for clinical efficacy." ✦

PRIORITIZE A RIGOROUS STRATEGIC PLANNING PROCESS

CLARE COLLETTI
■ *inVentiv Advance Insights*

Strategic planning is the key process that brings together functional area teams and activities into a single, well-orchestrated manner and is essential whether a company has just one product or hundreds. A thoughtful strategic plan serves as a framework for achieving consensus on strategies and a vehicle for communicating them across the organization. Through rigorous analysis and planning, companies can identify the most effective strategy for getting the right product to market, and maximizing commercial opportunity both for individual products and the entire portfolio.

Strategic planning can occur at any point in the commercialization process but should be developed no later than Phase II development. Once formulated, plans should be thoroughly reviewed annually, or more frequently in the face of unexpected market events. The plan typically outlines market conditions and strategies over a five-year period, but may include a more detailed plan for the first year. Gaining executive support is critical, either by actively engaging management in the process or through empowerment of the planning team to make decisions.

Cross-functional consensus is key

The strength of the plan substantially depends on projections of future market behaviors and competitive activities. The planning process should be a highly interactive activity that draws upon expertise across functional areas to accurately predict not only changes in physician, patient, and competitor behavior, but also trends among the "influencers" such as managed markets, regulatory bodies, government entities, and advocacy groups. Taking a collaborative approach also facilitates greater integration and coordination of various groups during the implementation of the plan. The strategic plan should be a living document that is referenced frequently to maintain alignment.

Align the organization around the plan

A strong strategic plan is important, but it is of limited value unless the organization is properly aligned to execute it. There are two basic approaches to aligning the organization around common strategies and objectives. First, it can be accomplished structurally by establishing permanent planning teams composed of individuals who are responsible solely for strategic planning for new products. Alternatively, the planning function may be driven by a cross-functional team, each of whom has strategic planning responsibilities in addition to their primary job function.

Achieving and maintaining alignment around plans is always challenging. One way to advance the process is to ensure that the plan is not shelved after it is completed. Rather, the plan should be posted, updated annually, circulated and referred to frequently in the course of business. Whether plan ownership resides with a permanent portfolio or planning organization or a cross-functional team, team members will move in and out as people move around the company. When a new individual takes on a role on a planning team, the plan itself is the tool by which to orient the new member and renew the overall team's commitment to the plan.

Whether a company has a centralized planning hub or a more loosely affiliated cross-functional team, the goal will be the same. Individuals across functional areas with diverse, and often conflicting goals and agendas, must coordinate their plans into a single cohesive set of objectives and strategies. The key ingredient is objectivity. Whether this is available internally or outsourced, objective thinking and tools that are standardized across the company provide a means to transcend politics and personalities and make decisions of greatest benefit to the organization.