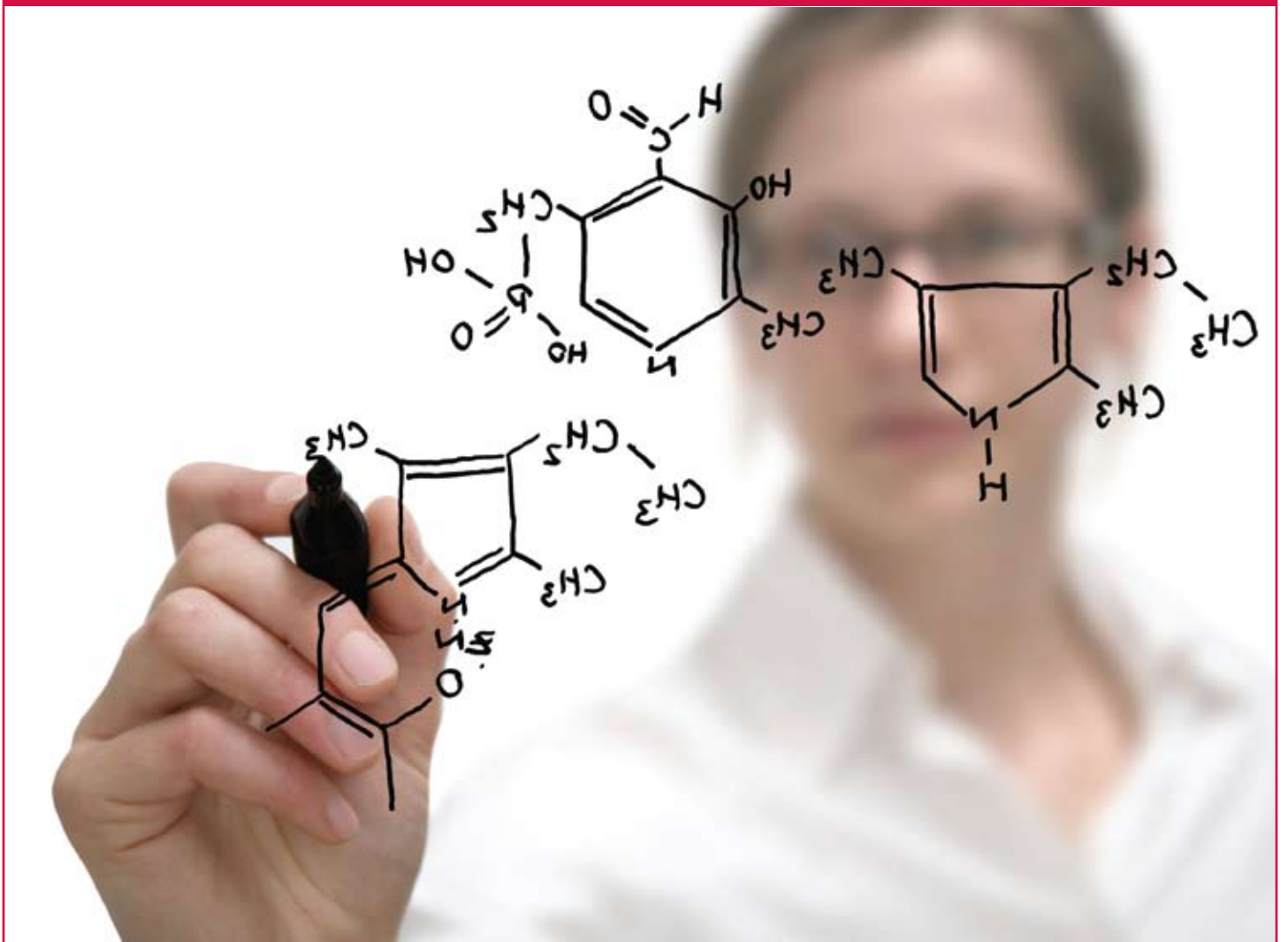


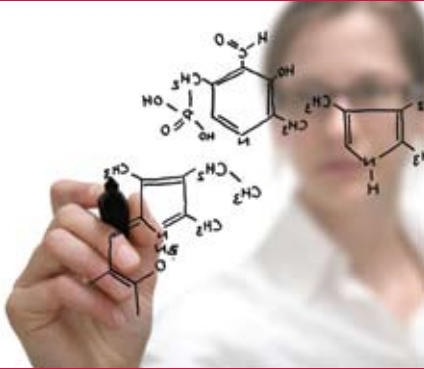


Quintiles Executive Vision Forum

Shaping Clinical Transformation



Overview



Speakers Highlight Transformation and Virtual Pharma

In the face of clear evidence that “business as usual” is no longer an option for the biopharmaceutical sector, companies are exhibiting an unprecedented willingness to share experiences and ideas for solutions to industry-wide problems.

Some key questions surfacing in the dialogue include: Are productivity, cost and timeline trends continuing? Are they universal? Is the old business model irreparable? Are any of the new business models working? What transformations to clinical development are emerging from the crucible of industry change?

This and other questions were discussed by executives from the world’s largest pharmaceutical and biotechnology companies at an event in Princeton, New Jersey, on September 15, titled *Shaping Clinical Transformation*. The event was part of Quintiles’ *Executive Vision Forum* series, developed to provide industry leaders with opportunities to speak candidly about some of the most pressing challenges facing the biopharmaceutical industry today.

To follow are key insights from the Executive Forum, based on speaker presentations and question and answer sessions.



Key Insights

>> Pharma companies are often unable to initiate current programs, resulting in the latent value of drug portfolios not being realized...

Shrinking Returns from R&D Expenditure

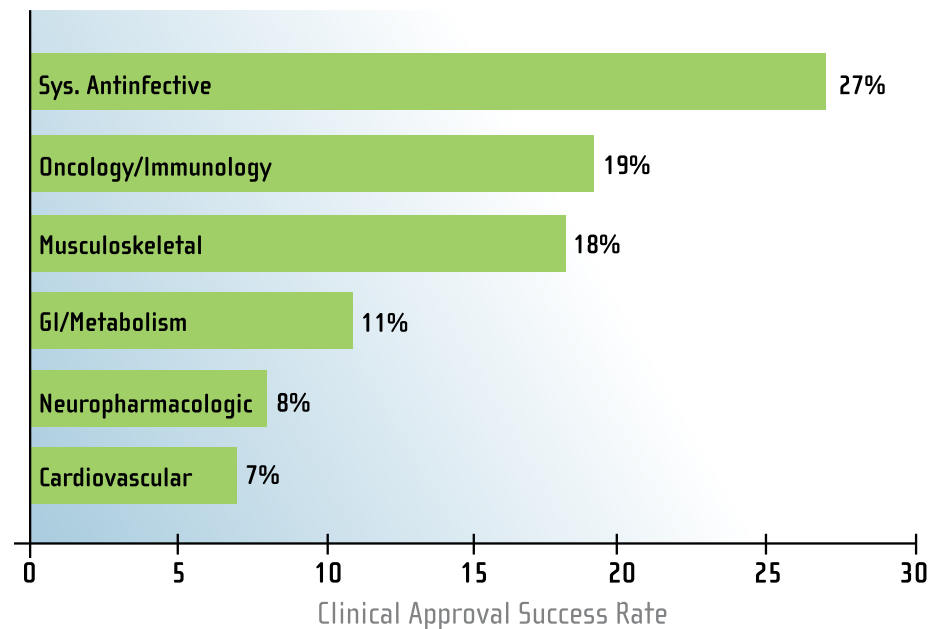
NDA approvals are at historic levels but expenditure is at an all time high.

Kenneth I. Kaitin, Ph.D., Director and Professor of Medicine at the Tufts Center for the Study of Drug Development (CSDD), highlighted the fact that returns from R&D investment continue to diminish. Kaitin said that only three out of 10 approved drugs recoup their average R&D costs, concentrating the economic viability of companies in a few products, and increasing their exposure to exclusivity loss. In addition, for the first time, there was a decline in R&D investment (expressed in constant dollars) in 2006 and 2007.

The shorter approval times that followed passage of the Prescription Drug User Fee Act (PDUFA) in 1992 have been canceled out by longer development timelines, and new drug approvals are not keeping pace with R&D spending. One example is the oncology (antineoplastic) therapeutic category, which accounts for about 30% of global R&D spending, and now takes nearly nine years on average from Investigational New Drug (IND) filing to New Drug Application (NDA).

This trend increases the impact of any particular drug on both the development budget and the fixed resources of the development organization. Consequently, pharma companies are often unable to initiate current programs, resulting in the latent value of drug portfolios not being realized as drugs wait on the shelf due to increased development costs.

Overall Clinical Approval Success Rates for NCEs Has Dropped to 16%



Source: Tufts CSDD Impact Report, 11(4), Jul/Aug 2009

Key Insights

(Continued...)

>> Top performing firms employ several best practices. First, they focus on core competencies, with a higher level of outsourcing and prioritized use of resources.

Increasing Development Risks

Falling clinical success rates reported.

The likelihood that a drug entering clinical testing will achieve NDA approval is also decreasing, said Kaitin. The latest studies from Tufts CSDD have found a decrease in the overall probability of regulatory approval for drugs entering the clinic from 22% to 16% for New Chemical Entities (NCEs). For oncology drugs, the success rate is just 8%. In these drugs, the failure is on grounds of safety and efficacy, and is driven by the complexity of the clinical end-point and uncertainties around mechanisms of action. The situation is similar for cardio-vascular drugs, with a 7% probability of success. In contrast, the low success rate is due to lack of differentiation in a highly competitive and payor-oriented, cost regulated market.

The time, cost and risk involved in bringing a new product to market remain “formidable challenges” for the pharma industry, Kaitin concluded. This will continue to drive new R&D strategies, including reorganizations, partnerships, network relationships and targeted medicine development.

Safety and Efficacy No Longer Enough

Attrition in pharma companies' portfolios is increasingly due to market access and economic return factors.

Kaitin noted that 20% of products fail to reach regulatory approval for safety concerns (a figure that has remained the same for decades), while 38% fail for efficacy reasons (a number that is increasing). Some 32% fail for economic reasons, the fastest-growing reason for product failure. “This makes it clear that although safety and efficacy are enough to clear regulatory hurdles, they are not enough to compete in the marketplace,” Kaitin stated. Since product failure for market reasons tends to occur four years into product development—well into Phase III in most cases—withdrawing a product at this phase significantly contributes to increased development costs.

Best Practices of Top Performing Organizations

Kaitin also pointed out that top performing firms employ several best practices. First, they focus on core competencies, with a higher level of outsourcing and prioritized use of resources. Second, they collaborate actively with global regulatory agencies. Third, they take full advantage of e-data management technologies. And fourth, they make use of off-shoring.

A New Paradigm for Innovation

Creative financing and operational partnerships will significantly change the business model for most biopharmaceutical companies.

Kaitin said that in his 23 years with the Tufts CSDD, he has “never seen an environment where there is so much willingness among biotech and pharma to share ideas and concepts...and work together to improve the underlying process of bringing new products to market.” Kaitin noted that partnerships—industry-to-academia, pharma-to-biotech, pharma-to-

Key Insights

(Continued...)

Service providers and capital institutions are taking a bigger role in sharing risk with pharmaceutical companies, to allow firms to be effective, efficient and agile.

pharma, and novel arrangements with CROs, PE funds and other capital institutions—will play an increasing role in moving products through the development cycle.

Patent expirations are also adding pressures, Kaitin noted, with \$20 bn in sales forecast to be lost in 2009, \$12 bn in 2010, \$32 bn in 2011 and \$25 bn in 2012. “We’ll see a new paradigm for innovation that I suspect in the next five to 10 years will be very different from what we’re seeing right now,” said Kaitin.

A Taxonomy of Pharma Risk

Peter Payne, Vice President at Quintiles, described a “taxonomy of pharma risk,” noting that companies are now segmenting development risks into three distinct categories:

- **Portfolio risk**—the uncertainty related to harnessing a candidate drug’s inherent utility and value. This can be managed by optimizing pipeline value and hedging risk.
- **Operational risk**—the execution risk involved in delivering robust clinical information about a candidate drug. This can be minimized by improving operational efficiency and outcomes.
- **Resource risk**—the exposure arising from inertia in the fixed-cost base that supports operations. This can be handled by reducing infrastructure costs and variabilizing the workforce.

Service providers and capital institutions are taking a bigger role in sharing risk with pharmaceutical companies, to allow firms to be effective, efficient and agile, Payne said. Risk-based partnerships offer a promising way forward, providing structured access to resources, processes, systems and—via capital—compounds. They generally involve shedding the traditional large-scale, fully integrated business model and moving to a more nimble, modular and variable way of leveraging resources to increase the value of assets.

Taxonomy of Risk

KEY CHALLENGES

Effectiveness

- Bringing new products to market
- Addressing P&L pressures
- Increasing development bandwidth
- Overcoming market access hurdles

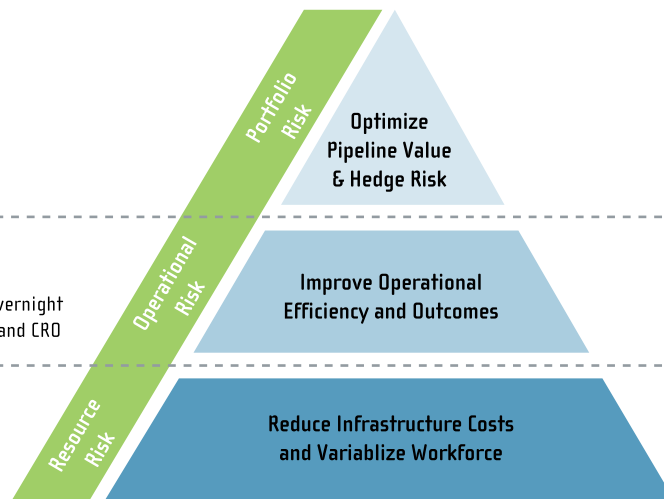
Efficiency

- Cutting development cycle time
- Reducing development expense and overnight
- Aligning incentives between sponsor and CRO

Agility

- Providing flexibility to respond to staffing needs and market pressures
- Efficiently managing and coordinating diverse functions

VALUE



SOLUTIONS

- Provide at-risk capital/services to stretch development budget
- Provide more “shots on goal” to release latent portfolio value
- Provide resource in peri-launch period to ensure launch excellence

- Transform models/processes to reduce variability/timelines/cost
- Increased development collaboration to reduce oversight and improve efficiency

- Provide large scale absorption & integration of functions (monitors, data management, sales forces, etc.) to variabilize costs and increase flexibility

Key Insights

(Continued...)

>> CROs today are increasingly prepared to share the financial risk of drug development with their sponsors, and be fully accountable for the execution of clinical projects.

From Provider to Ally

The relationship between sponsors and CROs is shifting to a full partnership.

Kaitin noted that the relationship between trial sponsors and contract research organizations (CROs) is evolving from a “standard provider relationship, which is more transactional oriented, to a more partnered or functional service provider or even an alliance approach.” This reflects the fact that “business as usual is no longer an option for the industry. In the last one or two years, a merging of operational and strategic objectives has taken place for the first time. You can’t have one without the other—both are now part of one process,” Kaitin pointed out.

According to Payne, CROs today are increasingly prepared to share the financial risk of drug development with their sponsors, and be fully accountable for the execution of clinical projects. Some agreements involve CROs taking a greater degree of control over the development process, but this does not necessarily mean moving towards a “big pharma” business model.

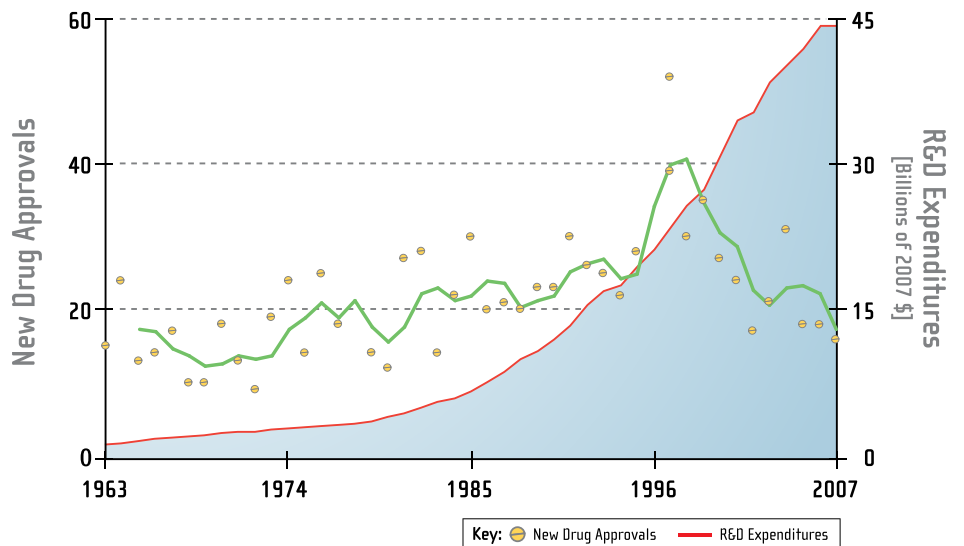
“When CROs start to take control of intellectual capital, then you may start to get into some muddy waters around conflict of interest,” Payne said. “However, CROs have a long history of managing perceived conflicts of interest—for example, working on several products within one therapeutic category. They have learned to handle this, leveraging their expertise and experience to the benefit of their sponsors.”

From Transactions to Trust

Sponsors trending toward relinquishing control over the execution of clinical development and relying on the partnering CROs expertise.

In tandem with the increase in risk-based partnerships, sponsors are beginning to alter the predominant mindset that they must retain exclusive control of planning and executing

New Drug Approvals Are Not Keeping Pace
With Rising R&D Spending



Source: Tufts CSDD Approved NCE Database, PhRMA, 2008

Key Insights

(Continued...)

>> Virtual Pharma is just one alternative the pharmaceutical sector can consider as an innovative step forward toward transformation of their business model.

the development strategy for a product. Payne identified an emerging trend to access more of the latent value in the portfolio by rebalancing the risk on operations by trading input to design for accountability for outcomes. “When I look back 10 years at outcomes-based contracting in the development space, it was very much a tool used to move risk, but not to cede control,” Payne said. “Companies are now gingerly treading back into this space on the premise that control over execution has to move along with the risk.”

Solomon Babani, Director of Outsourcing and Vendor Management with Celtic Pharma, outlined the evolution of relationships between sponsors and CROs. “What used to be transactional is now based on trust and relationships; what used to be tactical is now based on strategic planning; what used to be about managing inputs is now about managing outcomes. It’s a totally different type of interface, based on peer-to-peer interactions.” Setting up a risk-share arrangement so that the CRO is empowered to make decisions based on their own deep level of expertise will be the critical key for successful virtual drug development model. “You have to establish a relationship based on trust that will incentivize the CRO to carry out the clinical development plan to the best of their abilities,” Babani said.

Virtual Pharma

A promising option.

Virtual Pharma—in which all development work is outsourced—is just one alternative the pharmaceutical sector can consider as an innovative step forward toward transformation their business model. Babani described Celtic’s unique model of virtual drug development, saying that this involves a small core of highly experienced, internal, full-time professionals. These individuals collaborate with another small group of executives who manage execution through outside CROs and other vendors.

“Project leadership is critical, and should involve a combination of strategic and operational expertise, particularly in late stage development.” Babani crystallized the key challenge to the virtual pharma model is the need to close the gap between thinking and doing at the CRO. Key competitive advantages of a virtual pharma model include:

- **Innovation** (e-recruitment, remote electronic data capture, digital site monitoring and instant data-base lock)
- **Creativity** (virtual operating model, adaptive trial design and risk sharing)
- **Leadership** (modeling and reinforcement by a team which embraces change).

Summary and Conclusions

Adrian McKemey (who directs the Product Development and Commercialization consulting practice in QGC) summed up and concluded the forum with some observations on the nature of pre-competitive consortia on industry wide issues.

He highlighted that the aggregate data held collectively industry by bodies such as regulatory agencies, payers and CROs held powerful clues to operational and clinical matters that may not be apparent in the weak signals present at the individual company level.

He noted activity in a small group of interested players from across regulators, manufacturers, CROs and academia toward collectively addressing many of the issues discussed in the forum, and committed to connecting the participants to the ideas as they develop.

Speakers

Kenneth I. Kaitin, Ph.D., Director and Professor of Medicine at the Tufts Center for the Study of Drug Development (CSDD), is an internationally recognized expert on the science of drug development.

Peter Payne, Vice President of NovaQuest, a Quintiles company, is responsible for the development of relationships at a strategic level with a portfolio of pharmaceutical and biotechnology companies and Venture Capital funds.

Solomon Babani is Director of Outsourcing and Vendor Management with Celtic Pharma and Celtic Therapeutics, where he is responsible for implementing and overseeing the entire outsourcing process and strategy for all functions (pre-clinical, clinical, regulatory, manufacturing, etc.) within Celtic Pharma Development Services (CPDS).

Adrian McKemey is a Managing Director with Quintiles Consulting and leads the Product Development and Commercialization Practice.

About Quintiles Global Consulting

Quintiles Global Consulting works with pharmaceutical, biotech and medical device companies to maximize potential and minimize risk, from discovery through development and commercialization by providing expert strategic, operational, and technical advice. Building on the global reach and expertise of Quintiles Transnational, Quintiles Global Consulting practice areas include Product Development and Commercialization, Regulatory and Quality, Market Intelligence, Market Access, and Evidentials. For more information, please visit www.quintiles.com/consulting.

About Quintiles Executive Vision Forum Series

Quintiles' Executive Vision Forum series is designed to bring together senior biotech, and pharma leaders for thought-provoking discussions of industry-wide issues. The pharmaceutical industry is confronting systemic game-changing challenges to the fundamentals of the business model, with one of the key manifestations being transformational change in the value chain and operations. Events such as the Shaping Clinical Transformation forum provide a venue for industry executives and key opinion leaders to better understand the elements of clinical transformation required for a new health environment. For more information, contact Matthew.Eberhart@Quintiles.com.

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