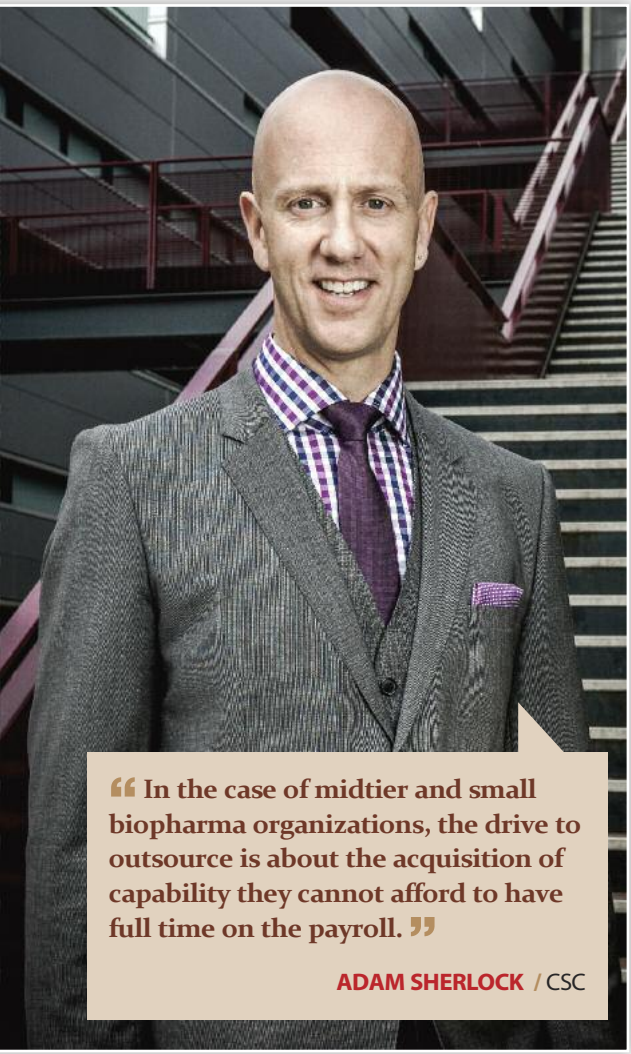
Denise Myshko

Outsourcing *Becomes* STRATEGIC

Pharma and biotech companies are now looking to their outsourcing partners to also weigh in on critical strategic and execution decisions.

Cost, time to market, and risk are causing more companies to reduce their reliance on internal R&D for innovation. Outsourcing R&D and buying the rights to smaller companies' products are common practice. Pharmaceutical companies are increasingly entering into long-term partnerships with other pharmaceutical companies, universities, and smaller biotechs for drug development.



> "In the case of midtier and small biopharma organizations, the drive to outsource is about the acquisition of capability they cannot afford to have full time on the payroll."
>
> **ADAM SHERLOCK** / CSC

Experts say the key drivers for companies outsourcing various R&D functions are cost, flexibility/scalability, and access to new/ different talent pools.

Previously, organizations outsourced the various functions to get a cost advantage, says Nagaraja Srivatsan, senior VP and head of life sciences, North America, Cognizant.

"Now more organizations are outsourcing to get the best innovation and collaboration with their outsourcing partners," he says. "The old model was to outsource a business process component. Outsourcers delivered the process at less cost and reasonable quality. Today life-sciences R&D organizations are looking at outsourcing as an innovation engine to get drugs not only faster to market but to get the information infrastructure to make better decisions."

Cost was the primary driver of outsourcing for a long time, but now it is a mixture of cost and expertise, agrees Alistair Macdonald, president of clinical development services at INC Research.

"As the industry realigns itself with much of the expertise in drug development migrating from the pharma side to the CRO side, we are seeing companies outsource more and more of the strategy, processes, and the actual clinical work to CROs," he says. "We have very much gone from being a helping hand to being a helping brain."

Jamie Macdonald, chief operating officer at INC Research, says one trend having an impact on R&D in 2013 is greater collaboration among sponsors, CROs, academic organizations, and patient advocacy groups, who all have a keen interest in ensuring that the R&D side of the industry is successful.

"This kind of collaboration, where objectives are more closely aligned, ultimately benefits all stakeholders involved by bringing more targeted new drug therapies to market on an accelerated timeline," he says.

FAST FACT

THE MARKET FOR DRUG DISCOVERY OUTSOURCING WAS $9.4 BILLION IN 2011.

Source: Kalorama Information

In fact, drug developers are forging new ways to work with academic medical centers to create the next generation of breakthrough medicines, according to a panel of leaders from the industry recently convened by the Tufts Center for the Study of Drug Development.

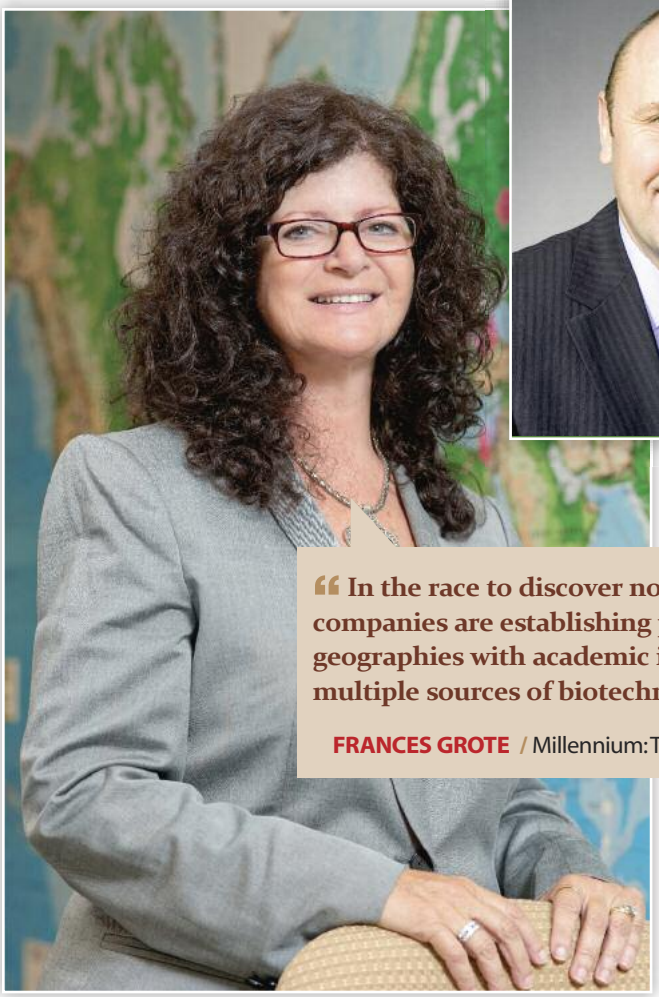
Executives at the roundtable concluded that working collaboratively often entails a cultural change for drug companies and their academic partners, as companies shift from spending money to buy molecules developed by others to co-investing and collaborating to discover new molecules.

Another trend, Jamie Macdonald says, is the evolving sponsor-CRO relationship, which seems to hold the most potential in terms of aligning objectives when it comes to delivering definitive outcomes within desired timelines.

"CROs have often been criticized for not being wholly aligned with sponsor objectives, but we're seeing more movement toward risk-sharing arrangements, where a series of milestone-based bonuses and penalties are agreed upon jointly by the CRO and sponsor," he says.

Jamie Macdonald says this is an area that will continue to evolve in 2013.

"We expect to see more partnership



> **"Contract research organizations have very much gone from being a helping hand to being a helping brain."**
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> **ALISTAIR MACDONALD** / INC Research

> **"In the race to discover novel compounds, many companies are establishing partnerships in low-cost geographies with academic institutions and with multiple sources of biotechnology research."**
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> **FRANCES GROTE** / Millennium: The Takeda Oncology Company

arrangements that align the success of the CRO more directly with the success of the sponsor," he says.

Frances Grote, senior director, clinical outsourcing, Millennium: The Takeda Oncology Company, says the factors that continue to drive outsourcing of various R&D functions can all be directly tied to achieving competitive advantage.

"Whether a company seeks to outsource to reduce its fixed costs — and thus increase its funds allocable to research — to purchase additional sources of novel compounds, to increase its access to druggable targets, or by some combination of the above, outsourcing, when managed strategically, provides a mechanism for expanding multiple resource pools," she says.

Ms. Grote says in the clinical trial execution space, outsourcing of at least some development activities has become the norm.

"Most drug companies have taken the position that maintaining a fixed labor pool to carry out the more transactional activities in clinical development, such as some of those in data management, is not an effective use of limited funds and resources," she says. "In addition, the need to engage investigative sites around the world entails infrastructure costs that are prohibitive for all but the largest pharmaceutical companies. Because CROs can distribute that infrastructure burden across multiple customers, they're better positioned to support the necessary personnel in multiple regions."

Scott Connor, VP of marketing at Acurian, says reducing overhead will always be a key factor in any outsourcing decision.

"But I believe specialization and expertise have jumped ahead in the catalyst queue when it comes to outsourcing within R&D and other areas of the pharma enterprise," he says. "Cutbacks in staffing have left pharma companies with voids in functional expertise that still have to be filled in order to move drugs through the pipeline. Companies with specialized services fill that void."

Mr. Connor says new development paradigms affected by technology and social media have left a knowledge gap within R&D organizations.

"Again, this has left R&D departments short on specialization, and there is too steep a learning curve for researchers to pull that expertise in-house," he says. "So there is an interesting intersection of cost cutting and drive for innovation that is increasing the demand for outsourced services that can bring efficiencies to the R&D enterprise."

Adam Sherlock, director of life sciences at CSC, says for big pharmaceutical organizations, the primary driver of outsourcing is to take cost out of their operations so that they are able to do more and do it more cheaply.

"In the case of midtier and small biopharma organizations, the drive to outsource is about the acquisition of capability they cannot afford to have full time on the payroll," he says.

Outsourcing Development Services

Experts say Phase II and Phase III trials have been traditionally outsourced the most because these are the most costly and most complex phases in development. For these studies, pharmaceutical companies often need patients from different regions, and vendors/CROs provide that global reach and access.

Cutting Edge Information has found that clinical research associates (CRAs/monitors) are the most frequently outsourced clinical operations function, says Ryan McGuire, research team leader at Cutting Edge Information.

"In our study, the average Phase IIIa trial employed 24.4 CRAs, 15.7 of which were outsourced," he says. "Data management, medical writing, and biostatistics activities are also frequently outsourced."

Mr. McGuire says Cutting Edge Information's study on clinical operations revealed that 63% of Phase II trial costs were outsourced, the most of any trial phase.

"Many large companies have such a high volume of compounds transitioning from clinical pharmacology studies into Phase II

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>
> **JAMIE MACDONALD** / INC Research

> "Companies are evaluating processes that they have taken in-house in the manufacturing life cycle and may decide that it is no longer a core competency."
>
> **FRAN DEGRAZIO** / West Pharmaceutical Services

that they need to rely more heavily on outsourcing," he says. "Most companies' development strategy calls for keeping important Phase III registration trials in-house if at all possible to keep a closer eye on things."

Ms. Grote says in the race to discover novel compounds, many companies are establishing partnerships in low-cost geographies with academic institutions and with multiple sources of biotechnology research.

"While some of these deals are true outsourcing, more and more companies are looking to establish alliances and collaborations that allow both partners to build multiple independent relationships," she says.

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>
> **RYAN MCGUIRE** / Cutting Edge Information

One company creating such alliances is Onyx Pharmaceuticals. N. Anthony Coles, M.D., president and CEO of Onyx Pharmaceuticals, says the company is creating strategic alliances with academic institutions and patient advocacy groups to enable the company to further explore novel experimental therapies and key molecular pathways in multiple myeloma and lymphoma.

"For example, in June, Onyx and the University of Texas MD Anderson Cancer Center announced a nonexclusive research alliance for preclinical and clinical research to understand the role that novel experimental therapies, including Kyprolis (carfilzomib) and oprozomib, can play in the potential treatment of hematologic cancers, including multiple myeloma and lymphoma," he says.

Dr. Coles says Onyx also has partnered with the Multiple Myeloma Research Foundation to create the first expanded access program for patients in six years.

"More than 300 eligible patients with multiple myeloma, many of whom had exhausted all available treatment options, were able to obtain preapproval access to Kyprolis before the medicine received FDA accelerated approval in July," he says.

Fran DeGrazio, VP, global research and development, at West Pharmaceutical Services, says as companies evaluate where to put their resources, it always makes sense to place those resources where the company is strongest from a core competency or technology standpoint.

"Companies are evaluating processes that they have taken in-house in the manufacturing life cycle and may decide that it is no longer a core competency and are outsourcing," she says.

Clinical monitoring and clinical data management have always been heavily outsourced, Alistair Macdonald says.

"As expertise shifts to the CRO industry, we are now seeing more study start-up work, contracts management, regulatory start-ups, and more," he says. "Biopharmaceutical companies have realized that CROs have global footprints and on-the-ground expertise to navigate local customs, regulations, and regulatory authority guidelines more efficiently, so there has been a considerable uptick in the outsourcing of this work over recent years."

Mr. Sherlock says over the last two years there has been an increase in the volume and scope of regulatory affairs and regulatory operations activities that are being outsourced.

"Until recently these were considered sacred cow functions that would never be outsourced, but the three competing demands of cost reduction, expansion of capability and increase in workload have forced the industry to look externally for support," he says.

Mr. Sherlock continues: "This sector has evolved along the maturity scale at breathtaking speed from initial tactical, project-based outsourcing of specific functions or operations to true end-to-end business process outsourcing where entire departments and functions are being turned over to the specialist external solutions and service provider."

Outsourcing Drug Discovery

Once an activity kept in-house at global pharmaceutical companies, the discovery of new compounds with a possible pharmacological effect is now increasingly handled by outside firms, according to a recent study by Kalorama Information.

With R&D expenditures declining, companies seek these services with the hope of developing more potential drugs out of limited spending dollars, thus creating a $9.4 billion market for drug discovery outsourcing in 2011, according to the Kalorama report.

Drug discovery has become increasingly complex as a result of advances in molecular biology and the emergence of new-generation biological therapies. These advances, plus the emergence of new technologies, have made it unsustainable for pharmaceutical companies

Outsourced Functions

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The study revealed that 63% of Phase II trial costs were outsourced, the most of any trial phase. Many large companies have such a high volume of compounds transitioning from clinical pharmacology studies in Phase II that they need to rely more heavily on outsourcing. Most companies' development strategy calls for keeping important Phase III registration trials in-house if at all possible.

Source: Cutting Edge Research

to undertake all drug discovery functions in-house, Kalorama researchers say.

Companies' overall budgets for discovery are declining as the cost for discovery is transferred across multiple players, says Mark Hronec, director, pharmaceutical R&D advisory service, at PwC.

"In addition, over the last several years, pharma has been putting more emphasis and resources in their late-stage pipeline to try to push more drugs on the market to offset those that are coming off patent," he says. "The long-term impact of this will be more collaboration between pharma, biotech, universities, and CROs to increase the probability of success and reduce risks and costs across the value chain of development."

Mr. Srivatsan says drivers for outsourcing discovery programs are costs, throughput, and the large amount of highly qualified talent needed to process results.

"The discovery process has become a brute force approach that aims to look at huge volumes of information and data and make the right analysis," he says.

This, Mr. Srivatsan says, requires a lot of time, talent, and effort.

"That is the reason why outsourcing of drug discovery is increasing," he says.

Mr. Hronec says sourcing strategies within drug discovery have evolved over the last several years.

"Pharmaceutical companies are moving away from conducting all of the research and discovery in-house to looking at universities and biotech companies to fill their early stage pipeline," he says. "The key driver in sourcing discovery programs is access to additional talent and expertise in particular and emerging areas."

Mr. Hronec says universities and biotechs are a hub for innovation.

"Companies will continue to create partnerships with these institutions to supplement their discovery efforts, as well as use new and innovative technologies, he says. PV

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Best Practices in OUTSOURCING

Industry experts discuss strategies for making sure outsourcing partnerships are successful.

Making an outsourcing relationship successful requires the partners to establish a clear sourcing strategy for the organization, functional area and/or department, says Mark Hronec, director, pharmaceutical R&D advisory service, at PwC.

"This includes identifying what is core and noncore to the business, followed by the identification activities that will be sourced and to whom," he says. "A best practice is to select a vendor that can not only conduct the activities that are to be sourced, but also fits with the organization culturally, strategically, and that has a willingness to partner. Another best practice is establishing a governance structure with both the vendor and the sponsor involved to ensure risk mitigation and quality. Finally, a fourth best practice is to have a comprehensive contracting framework with a detailed MSA and SoW comprising SLAs and clearly defined metrics to track performance as well as penalty and reward clauses."

Mr. Hronec says traditional pharma industry approaches to investment have evolved in order to reduce or share potential risks.

"This drive is evident in pharma's push to move away from transactional fee-for-service contracts with CROs to more collaborative models," he says. "This move should decrease investment risk born by pharma firms by driving third parties to provide more accurate financial forecasts and focus more on outcomes rather than just completion. Pharma firms have also employed a risk sharing approach when looking to in-license products, where acquisition is no longer the predominant model. Firms have been focusing more on co-developing compounds, which allows them to decrease their up-front investment, providing smaller milestone awards to fund the next phase of development."

Alistair Macdonald, president, clinical development services at INC Research, says a priority in building a successful relationship is a collaborative dialogue on needs, expectations, and capabilities.

"Pharma partners must be clear with their CROs about what they want from the relationship — is it a single trial, a full development strategy, or something else," he says. "In turn, CROs must make an honest assessment of their own capabilities. If the expectations and capabilities don't align, the relationship cannot work. That is why we spend a great deal of time in the 'definition' stage of relationship development with our customers. We also rely heavily on alliance managers, whose main responsibility is to remain close to customers, anticipate challenges, and help our internal team evolve along with the relationship to make sure we are always prepared to meet changing needs."

Adam Sherlock, director of life sciences at CSC, says outsourcing works best when the culture is set from the outset to be deeply collaborative for both parties — the sponsor and the vendor — with an implicit acknowledgement that it can't be a 'throw it over the wall' approach where the organization can simply

"Sponsor companies have moved away from the outdated notion that CROs need to be kept in the dark in order to guard confidential information. It is now widely accepted that CROs can contribute competitive and strategic intelligence to the drug development process."

FRANCES GROTE / Millennium: The Takeda Oncology Company

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offload their regulatory processes and walk away. It should also be accepted that, however successful the relationship, it is inevitable that issues and challenges will arise and that a joint approach will be needed to tackle them. Go into an outsourcing arrangement with these considerations in mind and you are more likely to match or exceed expectations.

According to Frances Grote, senior director, clinical outsourcing, Millennium: The Takeda Oncology Company, the critical outsourcing best practice is transparency between providers.

"This is a key success factor both for planning and execution purposes, as well as for building trust," she says. "Sponsor companies have moved away from the outdated notion that CROs need to be kept in the dark in order to guard confidential information. It is now widely accepted that CROs can contribute competitive and strategic intelligence to the drug development process, and that by sharing strategy and decision drivers, their CROs will be better able to contribute to success. In order to foster an environment of open communications it remains key to establish robust governance processes that engage both senior and middle management from both companies."

She says other best practices rely on standardization, pushing authority to appropriate levels of operational teams, joint and collaborative cost management, and proactive risk management. PV