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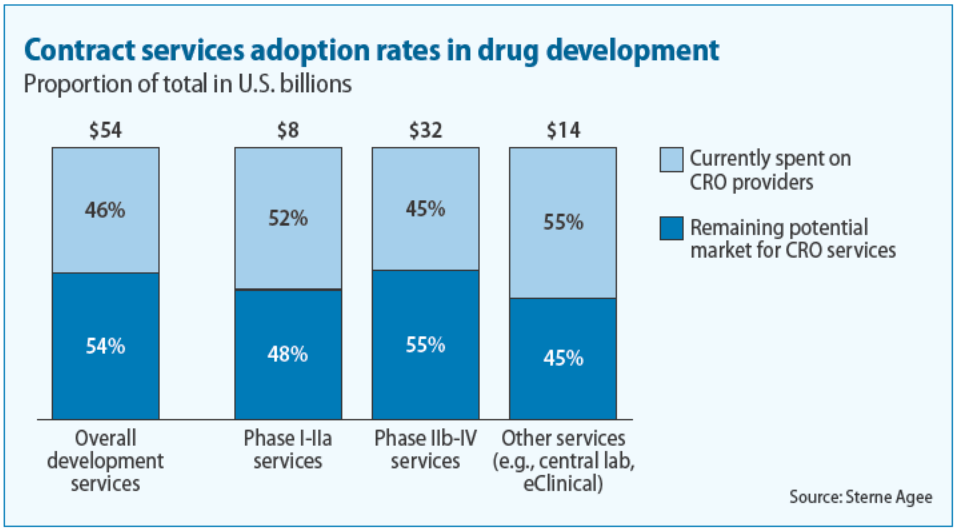
CRO market poised for growth and consolidation

Sponsors expanding pipelines, shrinking infrastructure fuel strategic outsourcing

By Karyn Korieth



CROs have seen strong financial results during the past 18 months, reporting higher revenue and a rebound in profit margins, and they expect another year of healthy growth fueled by strategic partnerships with sponsors and an increase in clinical outsourcing.

For publicly traded companies, strong earnings in 2013 drove stock prices higher, both public and private sources of capital continued to invest in CROs and the average profit margin in the clinical services sector, which fell to almost 12% in 2012, is expected to reach 16% next year.

And the outlook for continued growth in the CRO market, which reached $23.6 billion in revenue this year, is positive. Estimates from analysts at Goldman Sachs, which generally are consistent with views held by CRO management teams, forecast 2.3% global R&D growth from 2013 to 2016, which could drive 5% to 7% annual growth in the CRO industry. Outsourcing penetration rates are predicted to increase from an estimated 35% to 45%, to up to 60% or higher over the next five or six years.

Michael Martorelli, a director at Fairmount Partners, said the move toward outsourcing in R&D continues to grow as drug companies of all sizes increasingly appreciate the benefits of reducing their fixed costs.

"The failure rate in the drug world still is fairly high. If you have a whole battalion of clinical research people ready to go for your next phase III project and then your leading candidate fails in early phase II, what do you do with all of those people?" said Martorelli. "Substituting a variable cost for those fixed costs is the bottom line for what all of this is about."

Factors driving growth

An important driver in current CRO industry growth is a more favorable R&D market for both pharmaceutical and biotechnology. After a slowdown in 2009 and 2010, sponsors have ramped up development spending and are growing their pipelines. Large pharma companies have added new products through in-licensing and collaboration agreements with biotechs; consulting firm Deloitte found two-thirds of molecules in late-stage development at top pharma companies were in-licensed. In addition, the biotech sector has recovered as a result of new investments from both private equity firms and the capital markets.

As sponsors see stable or growing pipelines, they also are reducing internal headcount and restructuring their organizations to strategically outsource more of their clinical work to CROs. The industry, under pressure to reduce costs and improve development timelines, increasingly has outsourced its R&D work to improve flexibility, extend global reach and access additional expertise or capabilities.

"The industry is recognizing that having a really strong R&D partner they can outsource to and rely on is critically impor-

tant to their success, because they no longer have unlimited resources. In fact, most of them are looking for ways to reduce their resources," said John Watson, chief commercial officer and president, strategic partnering, at Covance.

The solid growth outlook for CROs, particularly the increase in profit margins, has attracted the interest of private equity investors over the past five years; Martorelli believes recent private equity acquisitions, such as KKR's purchase of PRA last year, have been a positive force in the continuing growth of the clinical outsourcing industry. And recent strategic acquisitions and partnerships carried out by CROs have helped drive up revenue.

Jamie Macdonald, chief executive officer of INC Research, said CROs have benefited from stability in the industry, as there have been no major acquisitions within the large pharma space in the past couple of years. Although there has been some recent movement in the market suggesting consolidation in the next year, Macdonald said the recent period of stability has allowed sponsors to "improve discipline" and take molecules and assets into late-stage development.

"We see the same sort of failure rates and attrition in development," Macdonald said. "But I think, by and large, the assets seem to be of better quality and we are running many of those programs through to completion and obtaining definite data on those trials."

Large CRO performance

Larger CROs, which have global scale and offer a broad range of services, appear to perform better in the market and report growth figures higher than the industry average. INC Research and Parexel, for example, both have reported 12% revenue growth. Most large CROs specialize in late-stage services and have benefited from the industry's focus on late-stage pipelines, an area in which sponsors outsource 47% of the work, according to estimates from Parexel management teams. In particular, massive global trials for diabetes research and cardiovascular outcomes studies for lipid-lowering agents or new classes of drugs have helped drive growth during the past year. Higher volumes of late-stage development also benefited Covance's central lab business, which grew 21% last year.

Revenue growth among the top 20 CROs also has been driven by strategic alliances formed with the largest biopharma companies during the past five years. As the role of CROs in drug development has grown, an increasing number of large sponsors have moved from transactional and functional service provider relationships into more integrated relationship models, in which partners manage entire development programs and sponsors provide minimal oversight and governance. According to Paraxel's Strategic Partnerships 2014 survey, which was conducted by an independent research firm, the strategic partnership model now is the dominant outsourcing approach for sponsors with R&D spending of $500 million or more; the survey also found more than half of biopharma companies in all geographies use strategic partnerships.

"Clients' needs are changing," said Covance's Watson. "As healthcare continues to evolve, clients are more often coming to us looking for solutions as opposed to just service. More and more people come to us and say they don't want to buy in individual pieces."

Many large CROs originally gave up profit margins in exchange for minimum levels of work from strategic partners and needed to build additional infrastructure to ramp up partnerships successfully. Fairmount Partners reports CROs have begun to see those investments pay off, as the average profit margins of the public companies it follows are rebounding back to the peak level—16%—they reached in 2009.

INC's Macdonald said initial investments in strategic relationships may have a short-term impact on profitability but, eventually, CROs find greater efficiency in those relationships and benefit from repeat work. Better cooperation between partners, greater transparency, deeper involvement in project planning and greater visibility into pipelines have allowed CROs to use personnel and facilities more efficiently, both in the U.S. and abroad.

"You start to find good ways to collaborate on things like the regulatory process, the site contracts process and the budget management pieces. You eventually get some efficiency and some economies of scale. In our larger relationships, we have pretty good line-of-sight on potential opportunities that will come our way, and that allows us to better manage and assign resources at an appropriate time," Macdonald said. "We also benefit when we see increased growth and repeat work. We get the advantages that come with economies of scale, better utilization, the better throughput and the better absorption of some of our fixed costs and investments."

Some companies also have implemented new strategies and programs to help improve margins. Parexel reported a 10.6%

Profit margins for publicly traded CROs are growing

	2012	2013
Quintiles	13.2%	16.0%
Covance	13.8%	15.3%
Parexel	11.5%	12.1%
Icon	10.5%	12.5%
WuXi	26.2%	27.0%

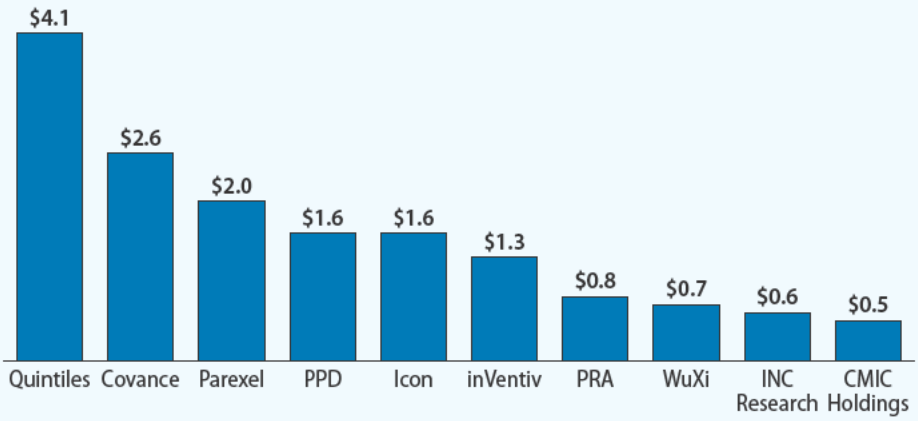
Source: Fairmount Partners (estimated EBITDA margins)

profit margin in its most recent quarter, an all-time record, and has seen profit margins expand for seven consecutive quarters. Parexel's decision to shift activities and resources from high-cost countries into lower-cost countries contributed to that increase; Parexel opened a service center in India where it performs typical support and back-office functions at lower labor costs. The CRO also began a number of "lean initiatives" by which small teams work to improve their areas, such as eliminating workflow activities that don't create value for clients, and it made a significant investment in IT infrastructure to automate and standardize processes.

"We have done a number of things that try to make sure we actually create a structure that gives us a sustainable way to improve margins going forward," said Ingo Bank, Parexel's chief financial officer. "Sometimes in the past we had ups and downs on our margins. For us it's important that we are able to continue and improve and not be patchy in our margin performances."

The largest global drug development contract service providers

2014 revenue in U.S. billions



Source: Fairmount Partners

Smaller CROs seeing growth

While CenterWatch analysis has found the 10 largest CROs dominate the market, contributing 75% of total contract clinical CRO revenue, the small and mid-sized players, far from being squeezed out of the market, also report solid growth and new hires. Many CROs with less than $100 million in revenue have developed niche services needed both by sponsors and other CROs.

Many small and mid-tier CROs have built service delivery and business models specifically to meet the needs of early-stage and mid-market sponsors, which typically lack internal infrastructure and, as a result, outsource high levels of clinical development. Small and mid-sized CROs have seen revenue increases as funding has returned to the biotech sector through private equity and IPOs. Trials that had been postponed or delayed when funding was slower now are moving forward and new biotech companies have emerged with new compounds. CenterWatch analysis found the percentage of the drug pipeline funded by small companies has jumped 23% since 2003 and now accounts for 65% of global development spending.

"R&D growth is coming back from biotech companies of all sizes, so CROs that can service these companies should be well positioned," said Andrew Schafer, president of Industry Standard Research.

Other CROs have followed the example of larger CROs and consolidated to build scale and geographic footprint. Mid-tier CRO Clinipace Worldwide, for example, has made several acquisitions to expand its global operations, most recently merging with Pan-Asian CRO Choice Pharma.

Clinipace, named to Inc.'s list of the 500 fastest-growing privately held companies for the past four years, reported a three-year growth rate of 918.55% from 2010 to 2012, from both organic growth and acquisitions. The company, which targets small and mid-sized pharmas and biotechs that have different needs and smaller budgets than large sponsors, expects growth to continue at the same rate this year due to increased business from both new and existing clients. As funding has increased in the biotech sector, many companies that previously focused their resources on a single compound and a single trial now are running multiple programs.

"For us, there has been an expansion in the business relationship because we are working with these smaller companies on multiple programs or multiple studies within the same program," said Mark Shapiro, vice president of clinical development at Clinipace.

Driving future growth

The ultimate penetration rate for outsourcing and which areas will grow most quickly are difficult to predict. Outsourcing penetration rates will vary throughout the industry, as some of the larger, faster-developing biotechs may morph into virtual development organizations, while pharma companies may decide to keep some clinical work in-house. Yet industry estimates of current penetration rates, which range from 35% to 55%, depending on whether discovery work or pass-through investigator and central lab fees are included, clearly point to room for growth in outsourcing going forward.

A report from brokerage firm Sterne Agee estimated nearly 100% of early development services could be outsourced, since these studies require "asset-heavy" resources sponsors would rather avoid, and the

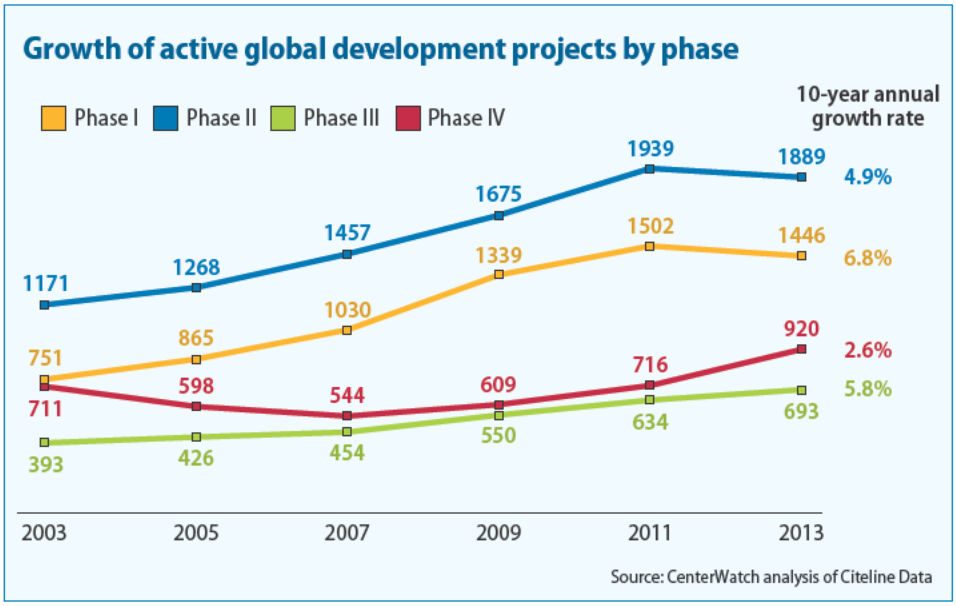
protocols for these studies are fairly straightforward. Meanwhile, the firm's analysts believe some phase IIb-III development will remain in-house, and the upper limit for outsourced late-stage services will be closer to 75%.

As the market continues to develop, top CROs have begun to launch new strategies and models to meet the needs of the pharma industry and continue to drive growth for their companies. CROs feel increasing pressure to offer their industry partners innovative solutions that can speed clinical trial timelines, improve site performance and predict study success.

Many CROs have focused innovation efforts on developing better ways to align technology with clinical development processes. Companies are integrating data collected at various points in clinical development—from feasibility and site identification to grants payment and pharmacovigilence—to reduce the need to enter the same data multiple times and to simplify clinical trial administrative duties.

Importantly, CROs also are using data and analytics to design scientifically and operationally feasible protocols, identify sites with eligible patients, speed patient recruitment and allow for better study oversight of the clinical development process. Covance, for example, is involved in more than 40% of clinical trials conducted because its clinical laboratory business has a high market share. As a result, the company has been able to compile a comprehensive investigator database it can use when selecting study sites and for other aspects of study management.

"We have data and insight on not only investigators and patient recruitment, but also the quality of the investigators. We know how many times they ship samples ambient when they should have been shipped frozen. We know how many errors they make on submission reports they send us. It really has helped drive our growth in the last few years, because we've had many, many situations in which we've taken the number of investigative sites that enroll zero to one patient from 55% down, in some cases, to single-digit percentages. That can reduce cycle times by months for our sponsors," said Watson.



Clinipace, which calls itself a digital CRO, has developed a software program that integrates data management, biostatistics, clinical operations, project management and safety data into a single system that provides real-time data, such as patient enrollment rates, and can increase visibility into site data during a trial. The company also is building sophisticated trial forecasting models that compare CRO and site performance to industry-wide metrics for a similar trial, and it has ongoing initiatives to develop technology that can connect software to site electronic medical records and other healthcare data.

"The industry always has generated data in a fragmented way, with the central focus being simply efficacy and safety data for regulatory submission. But in the course of generating that data, we generate at least 10 times more metadata about trials and trial operations. We've been trying to leverage and analyze that," said Shapiro. "I think there is room for the CRO industry not just to plug into the healthcare system more directly and access all of the data generated there, but also in terms of trying to understand itself as an industry, and the operational parameters. This goes way beyond metrics-oriented initiatives."

Many CROs are using technology and analytics to develop remote or risk-based models for monitoring trials. While programs vary from company to company, they typically use risk assessments and analytics to focus monitoring activities on sites that have the greatest potential to affect patient safety and data quality. The model is seen as a way to use clinical trial monitors more efficiently, improve site performance and data quality and reduce costs.

"CRAs no longer spend their time on site pursuing and addressing a standard list of issues," said Lori Eberhardt, vice president of remote site monitoring at PPD. "Instead, they now are able to target their time to working with individual study sites to assess specific process weaknesses to avoid future errors and deliver high-quality results."

Relationships with sites critical

CROs also consider their relationships with investigative sites as a critical success factor going forward. Site performance, particularly patient recruitment efforts, remains one of the greatest areas of inefficiency in

clinical research. Yet sponsors expect high levels of efficiency and performance when handing site management responsibilities over to their CRO partners.

Across the industry, various CROs have adopted numerous strategies and initiatives to improve relationships with sites. Parexel, for example, has simplified its communications with sites by assigning them a single contact point rather than have investigators consult with a number of operational, clinical and medical staff members. PPD, which recently acquired patient recruitment firm Acurian, tries to ease patient recruitment burdens for sites by providing substantial numbers of pre-qualified potential patients and technology-enabled services that aim to reduce patient attrition. INC Research has collaborated with external providers to develop better social media tools for supporting site training and communication.

At inVentiv Health, "we have designed a comprehensive process that leverages predictive modeling technology to establish realistic enrollment goals for sites," said Otis Johnson, executive director, feasibility and clinical informatics. "We also are providing sites with resources and tools to support patient identification and engagement. The goal of our efforts is to reduce the burden on sites to find, enroll and retain patients in unrealistic timeframes."

Nuala Murphy, Ph.D., president of clinical research services at Icon, said online tools adopted at Icon have changed how the CRO instructs and communicates with site staff, measure study staff competence and support sites during monitoring visits. The tools offer self-paced training modules for site staff and allow the CRO to report site-training behaviors to sponsors.

"Innovation has as yet barely intruded into how clinical trial sites work," said Murphy, "but already we have seen through our investigator portal how applying technology in the right way can bring substantial benefits to drug development and patient safety."

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New outsourcing opportunities

Top CROs also are looking for new opportunities to expand outsourcing capabilities into areas sponsors historically have kept in-house.

Parexel recently launched a new service line focused on maintaining regulatory documents for approved products already on the market, an activity sponsors typically have kept in-house even though it can consume up to two-thirds of their regulatory resources. The CRO also has expanded its chemical logistics business, for which it sees growth opportunities in managing drug supply, providing storage for drugs and managing import/export documentation processes.

At Covance, one of the few CROs to offer end-to-end services including early development and central lab offerings, Watson said post-approval, commercial services are one of the biggest opportunities from an outsourcing perspective and are part of Covance's growth strategy. While safety and efficacy concerns traditionally have been a leading cause of drug failure, today sponsors also need to address the economic forces that could derail a new therapy. Covance's post-approval commercial services provide sponsors advice on how to demonstrate product value, global health and economics outcomes research and commercial strategy.

"There is no question that post-approval type activities are going to continue to grow because the financial pressure on the companies, in terms of reimbursement and being able to market their drug, is going to continue to increase," Watson said.

Looking ahead

The state of the CRO industry remains strong. Both analysts and CRO management project continued growth in both revenues and operating margins this year.

While the industry's revenue growth relies on how much sponsors plan to spend on R&D, which is beyond the control of CROs, Martorelli of Fairmount Partners said both large and mid-sized CROs could hurt their upward trend in margins by acquiring low-margin businesses as they look to expand services. CROs also need to tightly manage the cost of their corporate overhead and infrastructure, he said, and "resist the urge" to build too much capacity or give away too much profit margin in their strategic relationships.

"It was clear they had to give up some margin to get some of these 'guarantees' of more revenue," said Martorelli. "But now that has come back to where their margins are recovering, because their revenues are really coming through."

Karyn Korieth has been covering the clinical trials industry for CenterWatch since 2003. Her 30-year journalism career includes work in local news, the healthcare industry and national magazines. Karyn holds a Master's of Science degree from the Columbia University Graduate School of Journalism. Email karyn.korieth@centerwatch.com.