CROs
(Contract Research Organisations)
and other outsourced pharmaceutical support services
M&A drivers and trends

Hemavli Bali
Executive Director
Results Healthcare

Brigitte de Lima PhD, CFA
Results Healthcare

Carrie Yang
Senior Analyst
Results Healthcare

Please contact:
Hemavli Bali
hbali@resultsig.com
+1 646 747 6506
Twitter: @R_Healthcare

588 Broadway
Suite 1010
NY 10012

www.resultshealthcare.com
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Executive summary

In recent years, biopharmaceutical companies large and small have become increasingly reliant on the contract research organisation (CRO) sector and other clinical services specialists to provide research services across the breadth of their R&D operations. The financial crisis had a significant impact on CRO companies, with sponsors scaling back trial programmes, particularly in the early-stage segment covering preclinical activities and Phase I trials.

Improving industry fundamentals should drive healthy growth

However, the sector has been recovering, driven by the biopharmaceutical industry’s improving fundamentals. Most biopharma companies, the CRO industry’s most important customers, are now at the tail end of multi-year patent cliffs and are stepping up investments in their late-stage pipelines. This is expected to drive modest growth in biopharma R&D expenditure in the foreseeable future, following negative growth in four out of the past five years. In addition, biopharma companies are increasingly outsourcing R&D work to CROs, mainly to access new capabilities, shift fixed to variable costs, and improve their global reach. Together, these factors are expected to increase the share of outsourced services from the current 24-28% to as much as 35% by 2018, and more than 60% in the longer term. As such, the CRO market is expected to expand from an estimated $23-25b today to over $30b by 2018, reflecting a CAGR of 5-6%.

This is fuelled primarily by rising demand for late-stage services – Phase II-IV, central laboratory and consulting services – which account for approximately three-quarters of the CRO market.

M&A environment to remain dynamic

Biopharma’s growing need for broader geographic and therapeutic reach as well as scale bodes well for continued M&A activity in the space, as mid-size and small players join forces to reach critical mass and compete more effectively with their larger rivals. This is particularly relevant in light of the current trend among large biopharma companies to rationalise their supplier list to a more manageable number, and forge long-term strategic alliances with one-stop-shops boasting broad service offerings, including non-traditional capabilities such as health economics and outcomes research (HEOR), market access and pharmacovigilance.

The robust fundamental drivers fuelling CRO market growth and consolidation have, for a number of years, also attracted the attention of private equity investors and, more recently, the capital markets. This is reflected, for example, by the recent initial public offering (IPO) of Quintiles, the largest global CRO. Key features that make this growth segment of the healthcare industry particularly attractive to private investors seeking to realise high annual returns and exits within 3-5 years include: high visibility of revenues, excess cash generation, strong balance sheets and limited exposure to a number of risks that commonly affect biopharma companies, such as regulatory and reimbursement risks, as well as the consequences of healthcare reforms.

Strategic buyers and private equity investors alike have been driving deal activity

While M&A continues to be driven primarily by strategic buyers looking to increase scale or add capabilities they do not currently have in-house, it is often the private equity deals that make the headlines, often because of their sheer scale and the impact they have on the industry. Two important secondary private equity transactions completed this year that should substantially change the CRO landscape are KKR’s purchase of PRA International and Research Pharmaceutical Services (RPS) in June and July, respectively. The two companies have been
merged to create a top-tier CRO player, but also, potentially, to follow Quintiles’s ‘buy, build and IPO’ roadmap. This deal is fundamentally different to the purchase of Pharmaceutical Product Development (PPD) by a consortium of private equity firms, including Hellman & Friedman LLC and The Carlyle Group, in October 2011, which was one of the last few deals completed at a time when CROs were struggling with the negative macroeconomic environment. Beyond full service CROs, private equity has demonstrated appetite for other specialist outsourced services, for example JLL Partners’ purchase of BioClinica and CorLab Partners in January, which the private equity firm intended to merge to create a leading provider of medical imaging services and eClinical solutions for clinical trials.

Smaller, yet important, deals completed during the past year by strategic acquirers looking to add specific capabilities include: Quintiles’ purchase of Novella in August 2013 to expand its oncology, medical devices and diagnostics offering; Parexel’s acquisition of market access consultancy Heron; and the merger between Synteract and Harrison Clinical Research (HCR), which formed SynteractHCR, a leading global CRO with strong capabilities in patient recruitment. The latter also highlights private equity’s interest in service companies that provide services to both CROs and sponsors, with Synteract backed by Gryphon Investors since September 2008. Another example in this respect is PPD’s acquisition of Acurian, a provider of patient enrolment and retention solutions, in August 2013.

**Specialised service providers remain a key area of focus for larger players**

Results Healthcare expects M&A activity in the CRO space to remain buoyant, particularly with regard to the highly fragmented CRO services support market, which includes hundreds of specialised companies that have emerged to address specific gaps in the CRO service offering. Segments that are in particularly high demand range from medical communications and patient recruitment to HEOR and pharmacovigilance. Healthcare IT is also a major focus, as CROs look to increase efficiencies across the board. Key areas include technologies that allow for real-time access to data, cloud platforms, and the use of mobile devices to simplify the collection of data.

**Scope of this report**

As well as providing a background to the field, this report looks at the different sectors of the CRO market, from clinical trials support functions to marketing and pharmacovigilance services. It also analyses the drivers behind the various market trends, and provides an overview of a selection of key deals completed in the past few years. Finally, it highlights the future prospects of this dynamic, developing and growing market.
Background to CROs and key service providers

CROs support the life science R&D process

CRO stands for contract research organisation, although it is often also used for clinical research organisation; this report focuses on the former. CROs provide drug discovery and development services to the pharmaceutical, biotechnology and medical devices industries, collectively referred to as sponsors. These sponsors hire CROs to facilitate activities across the R&D continuum. Hence, CROs obtain the majority of their revenues from sponsor R&D budgets, with work conducted by them in the form of short- or long-term contractual outsourced services.

Major benefits for the sponsor

Sponsors choose to outsource R&D activities to CROs for a variety of reasons, but particularly to access capabilities not found in-house, shift fixed to variable costs, and achieve greater global reach and scale. An overview of the key benefits to sponsors is provided in Table 1.

Table 1 Key benefits to sponsors

<table>
<thead>
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<th>Benefits</th>
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<td>Access to capabilities (e.g. therapeutic expertise) not found internally</td>
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<tr>
<td>Reduction of fixed costs and internal resource utilisation, shift to variable costs</td>
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<tr>
<td>Improved global reach and scale</td>
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<tr>
<td>Quality of and greater efficiencies in execution</td>
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<tr>
<td>Reduction of level of required sponsor oversight</td>
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<tr>
<td>Risk mitigation</td>
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<tr>
<td>Acceleration of time to market</td>
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<tr>
<td>Access to innovation not found internally</td>
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The two most important factors that influence a sponsor’s choice of a CRO include history of quality and cultural fit, according to Parexel’s ‘Strategic Partnerships 2013’ report. A partnership approach and cost considerations are also considered important, while technology and innovation are currently at the bottom of the list.

Late-stage services account for the lion share of revenues

Late-stage development work accounts for the bulk of CRO revenues, as it covers the larger Phase II–IV clinical trials plus central laboratory services. With regulators demanding more and larger trials, this is only likely to grow, in contrast to early-stage work, where trial sizes are small and unlikely to change significantly. For example, Covance has said that late-stage trials account for two-thirds of its revenues and 80% of its operating profits. Bank of America Merrill Lynch estimates that the market size for late-stage services is about three times that of early-stage work.

The combined impact of the global financial crisis, the wave of patent expirations and the mega on the biopharmaceutical industry had a detrimental effect on the overall CRO industry. However, early-stage players were hit harder as a result of their greater dependence on the biotech sector. Biotech companies were impacted by a significant downturn in the availability of funding, reducing the number of early-stage trials trials that they able to run.

Early-stage segment recovering more slowly from recent downturn

The late-stage development segment has been recovering more quickly, both in volume and value terms, due largely to pressures in the biopharmaceutical industry having led to an increased focus on projects that are further down the development pipeline. This has left the early-stage segment hampered by limited pricing power and sub-optimal capacity utilisation.

Large pharma remains the key customer group

Pharma and biotech are CRO’s key customer groups. As a result of their greater R&D budgets and the fact that they carry out the lion’s share of expensive late stage trials, large pharma companies account for the majority of revenues, particularly for the larger CROs. CROs prefer larger clients, as they provide more consistent, and a broader spread of, business. Smaller companies, meanwhile, offer more piecemeal business, as they often only outsource certain portions of clinical trials, and later stage trials are frequently partnered with large pharma companies.

Smaller companies fill the gap

The slow improvement in the market has led to a growth in demand from small and emerging clients for services from CROs. Increased funding in the biotech sector in particular has led to a rise in biotech companies seeking CRO services. Another area of growth is the medtech sector, with some CROs increasingly focusing on this untapped market.

Biotech spending is now at its highest level since the financial crisis hit in 2009. With cash in hand, the small-to-mid-sized pharma companies are looking to advance their projects.
through the clinic. Indeed, the mid-tier companies are currently having more commercial success, and are increasingly buoyant about their pipelines. This is in contrast to big pharma companies, where the situation remains challenging, although recent sector reports suggest that R&D productivity may finally be turning the corner.

**Rising customer concentration as a result of strategic partnerships and M&A**

A major trend in the CRO industry has been the signing of strategic alliances between large pharma companies and top-tier CROs, with at least 20 major deals signed in the last five years alone. While this has clear benefits for CROs (please refer to page 13 for further details), a key disadvantage is that it causes an increase in customer concentration. For example, in a recent quarterly earnings call, Parexel noted that its top 5 clients accounted for 50% of its service revenues, up from 40% a year earlier, with its top 20 clients responsible for nearly 80%. In addition, Parexel’s largest client accounted for 17% of service revenues, nearly double the proportion it had been the year before.

Rising customer concentration, which can also result from M&A activity, can be particularly detrimental for smaller players, as they can become very dependent on one or a few customers. In addition, strategic partnerships can result in less flexibility to cope with project cancellations because of this over-dependency on a limited number of clients, as staff cannot easily be redeployed. With such contracts usually being agreed on a fixed-price basis, CROs are likely to end up bearing the cost of any overruns. One way around this would be to include risk-sharing terms or guarantees on costs and timelines in future contracts.

**CROs rely on a variety of specialised service providers**

Many different drug development services companies support both CROs and sponsors. They tend to operate in specific silos, and are usually highly specialised. This section provides an overview of service areas that are currently in greatest demand and which have therefore experienced significant M&A activity in the past few years.

**Patient recruitment and retention remain the most intractable challenges**

Slow recruitment or inadequate retention of trial subjects is a leading cause of study delays and, hence, an overall increase in clinical trials cost. According to 2003 figures from the NIH, even a decade ago, when fewer and smaller trials were being run, an estimated 85% of trials were delayed due to recruitment issues. Trial delays are particularly detrimental for small companies such as biotechs, which often rely on one or a few drug candidates, and whose valuation and cash resources can be severely impacted by a major trial delay.

**Recruitment**

According to a study published in early 2013 by the Tufts Center for the Study of Drug Development (CSDD), based on 150 clinical studies involving nearly 16,000 sites, 11% of sites in a given trial fail to enrol a single patient (IMS data puts this figure at 27%), 37% under-enrol, 39% meet their enrolment targets and only 13% exceed their targets.

**Retention**

Poor retention has a negative impact on the overall evaluable data for regulatory submissions, as it may threaten the overall validity of the results, particularly when dropout rates exceed 20% per treatment arm. In some cases, dropout rates can be as high as 40%, which can be a reason for trial abortion. Some reasons for subject dropout are within the control of study staff, but most are not. These include primarily adverse events, but also issues related to convenience, such as dosing regime and mode of administration. Inevitably, patient retention can never reach 100%, but needs to remain within the assumptions made during study design.

A number of strategies can be employed to improve efficiencies. For example, eliminating low-enrolling centres and placing a greater focus on those with stronger enrolment figures can help ensure that a trial progresses as scheduled. This retains the potential value of the product to the originator company, as bringing a product to market on time allows it to achieve revenue expectations ahead of patent expiry. Consequently, it also ensures a positive net present value (NPV) of the product for the company.

Several types of organisation have sprung up to improve this part of the clinical trial process. They generally fall into the following categories: site management organisation (SMO), integrated site network (ISN) and patient recruitment and
retention provider. In some cases, only one or a few companies are represented in each category, reflecting the fact that there are only small differences in the type of services the companies provide.

Efficiency and successful enrolment are key, so building a reputation for reliability in patient recruitment is important and provides a barrier to entry to new players. Networks are being formed and are increasingly trying to integrate to improve their processes. They will be audited by their sponsor clients, and they want to be able to ensure the same standards in each of their sites, which are usually run autonomously.

**Site management organisation (SMO)**

SMOs represent a relatively new segment of the field that experienced rapid growth in the US in the mid-1990s. The sector developed in response to a highly fragmented and inefficient clinical trials marketplace, with SMOs emerging to improve efficiency. SMOs aim to provide economical conduct of clinical trials for their clients, with a focus on the management of clinical research sites. They usually have (and in some cases own) a network of clinical research sites that they manage and work with on a dedicated basis. They may manage all or just part of the clinical research activity at a clinical research site, which may be a hospital or a private practice.

Some of the services offered by the SMO include project feasibility, investigator selection, submission of documents for Institutional Review Board or Independent Ethics Committee (IRB/IEC) approval, patient counselling, patient recruitment, patient follow-up, and the translation of informed consent forms (ICF) into local languages.

Many of the early US entrants subsequently failed, largely as a result of their inability to successfully implement their business model, and only a few players now remain. SMOs have grown in importance in emerging markets including India, China and Brazil, where clinical trial activity is experiencing rapid growth. Estimating the SMO industry presents a challenge of its own because the amount of publicly available data is limited, but various industry sources put this figure at about $3b, with expectations for further growth.

**Integrated site network (ISN)**

ISNs are fully integrated networks of sites, with the networks’ operations solely dedicated to clinical research. Typically, they consist of private physician practices and other medical facilities, with the network providing guidance, consulting and training to these sites to help ensure timely and successful clinical trials. They developed largely as a defensive response to the emergence of SMOs. By integrating, they collectively offer sponsors and CROs some of the efficiencies of an SMO while preserving some autonomy. In practice sponsors and CROs prefer to deal with one centralised site, as it is simpler for them. The advantage of an ISN is that the sponsor running the trial is not exposed to the risk of only using one site; rather, they can benefit from a similar service provision across the whole network, which is also easier for risk-based monitoring.

**Patient engagement solutions can help improve recruitment and retention**

Patient engagement solutions are designed to support patient retention, for example by using websites or text messages to keep patients informed and motivated to remain in clinical trials. Technology is particularly important here, with modern communication methods and devices now having a real impact on patient buy-in to the study.

Examples of technology-based patient engagement solutions include:

- Study-specific websites, which provide a way to maintain contact with patients, offer on-going support and information, and allow participants to share personal experiences;
- Text messages sent via SMS that allow study centres to interact directly with subjects, providing customised visit and medication reminders;
- Interactive Voice Response (IVR) technology is particularly useful with older patients who may be happier with this type of interaction rather than using the internet or a smartphone.

**Market access, health economics and outcomes research remain in high demand**

The increasing influence of payers, whether governments or health insurance companies, has led to significant growth in demand for market access services. Reforms that are being made to healthcare systems in countries such as the US are also having an impact.

Payers make decisions on whether they are prepared to pay for any particular drug after considering its safety, efficacy and the value it provides. Increasingly, they rely on data collected from patients in the real world as well as clinical data collected during development when making those decisions. Randomised controlled trials used to be the most important information taken into consideration when making those decisions, but increasingly they are taking into account evidence collected from routine medical use in patients.

**Market access services**

Growing numbers of pharma and biotech companies are looking to outsource market access services, particularly those smaller biotech companies who may only have a single product and thus in-house capability would not be cost-effective. However, medium to large companies are also outsourcing this work in a search for flexibility, as well as experience in therapeutic areas where their own may be limited.
**Health economics and outcomes research (HEOR)**

Nowadays, economic endpoints are more likely to be included in Phase III trials alongside clinical endpoints, in order to demonstrate the cost-effectiveness of a new medicine. This has led to a rise in demand for companies offering outcomes research and comparative effectiveness research in order to assist in implementing these aspects into clinical studies. The growing reliance of the regulators and payers on healthcare economics data has led to a lack of commercial viability becoming one of the most common reasons for the failure of a new drug. Payers are increasingly looking, where possible, to provide medicines only to the subset of patients who would be most likely to benefit from them. This provides a rich vein of opportunity for companies specialising in the field of outcomes research.

This sector has seen significant acquisition activity in the past year or two (Table 2). There are only a few big independent companies remaining, and the huge interest of CROs in this space has led to high multiples paid on deals.

**Table 2 Recent acquisitions in the HEOR space**

<table>
<thead>
<tr>
<th>Date</th>
<th>Comment</th>
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<tbody>
<tr>
<td>Jul-2013</td>
<td>Symphony acquired several divisions of UBC, including health economics, health outcomes and market access, forming the independent portfolio company Evidera for an undisclosed sum. Results Healthcare advised Evidera shareholders.</td>
</tr>
<tr>
<td>Apr-2013</td>
<td>Parexel acquired Heron for $38.2m.</td>
</tr>
<tr>
<td>Dec-2012</td>
<td>DRG acquired Abacus for an undisclosed sum. Results Healthcare advised Abacus.</td>
</tr>
<tr>
<td>Jun-2012</td>
<td>McCann Health, part of IPG, acquired Double Helix for £50m.</td>
</tr>
<tr>
<td>Mar-2012</td>
<td>GfK acquired Bridgehead for an undisclosed sum. Results Healthcare advised Bridgehead.</td>
</tr>
</tbody>
</table>

Source: Results Healthcare research, company press releases

**Pharmacovigilance: another area of significant growth**

There are growing concerns among the regulators about serious side effects that only become apparent after a new medicine is used in very large patient populations. This has led to a significant rise in the importance of pharmacovigilance. Regulators commonly insist that a pharmacovigilance plan be put in place for any medicine that is new to the market to ensure that any such issues are picked up as quickly as possible, and pharma companies are increasingly looking to outsourced providers to help them manage these activities.

The European Medicines Agency (EMA) published a new European guideline on pharmacovigilance in 2012, replacing the earlier directive. The good pharmacovigilance practice (GVP) modules have yet to be finalised and, in some cases, remain transitional measures. Two key areas of focus include:

- A push for electronic submission, which has become a main driver for deals in the pharmacovigilance arena;
- The evaluation and management of safety signals, i.e. a new or known adverse event that is potentially caused by a medicine and that warrants further investigation.

Pharma companies are increasingly adopting signal management solutions to support their risk management activities, with risk evaluation and mitigation strategies (REMS) as well as risk management programmes (RMPs) becoming more widespread. Overall, pharmacovigilance activities are now being implemented much earlier in a product’s development. In the past, a drug’s safety and efficacy was commonly assessed once it reached the market and while it remained on sale. In contrast, nowadays an on-going risk/benefit analysis takes place throughout the product’s lifecycle, starting from the initial first-in-human studies, thus satisfying demands from the regulators.

**Contract safety organisation (CSO)**

The market for CSOs has been evolving over the past five or six years, with a particular focus on pharmacovigilance. In the early days, demand was largely driven by cost containment factors. However, the main reasons for using a CSO nowadays are more value-added around increasing safety. While the large CROs have wide expertise in regulatory aspects and are therefore well placed to offer pharmacovigilance advice, a number of niche CSOs have also sprung up in recent years to provide specialist knowledge and services in this area of growing importance.

**eClinical and technology enabled consultancy solutions having a huge impact**

eClinical solutions are making a huge impact in the market because of their ability to streamline information handling and increase efficiencies. They are electronic systems designed to automate the management or conduct of clinical trials, with the ultimate aim of replacing manual, ad hoc or paper-driven methods. The original meaning covered any technology application used within a clinical trials setting, such as electronic data capture solutions, clinical trials management systems, or randomisation and trial supply management systems. eClinical solutions often use interactive voice response systems, electronic patient diaries and other common types of electronic solutions.

However, the current usage of the term eClinical is more specific than merely referring to any form of technology employed in a clinical trials setting. It is now commonly used to represent the concept of integrated technologies in clinical trials (see Table 3 for examples). Many advantages are gained by the use of various pieces of technology together. Data is shared much more readily across applications, duplication of activities can be avoided, and the streamlining of multiple technologies gives real advantages of simplicity to those running the studies and analysing data. Many of these tools are web-based, because of the huge advantages an internet portal has in the sharing of information. Ultimately, eClinical solutions save time and money by adding efficiencies,
and make compliance with the regulators’ audit trail and security demands more straightforward.

Table 3  Key clinical technology applications

| Budgeting and benchmarking tools |
| Business analytics |
| Clinical trial management systems |
| Electronic data capture |
| Electronic patient reported outcomes (ePRO) |
| Protocol design |
| Randomisation and trial supply management |
| Site quality management |

Source: Credit Suisse CRO Industry report, 2013

Five key areas of interest for CROs in the eClinical field are reviewed in more detail below.

**Real-time data access allows for faster intervention**

A study from the Tufts Center for the Study of Drug Development published in October 2012 indicates that contract support and technical service providers are expected to play a greatly increased role in drug development in the future. By gaining access to data in real time, those running clinical trials are given a much better insight into how the trials are running. It means that any problems that might occur can be pinpointed – and fixed – much more quickly, allowing for tactical decisions about trials to be made while they are on-going. This is particularly important in light of the increase in adaptive trial designs (please refer to page 14 for further details).

**Cloud platforms enhance data efficiencies**

Research networks are increasingly being moved to R&D cloud platforms. The data efficiencies they afford are significant, as long as people’s concerns about confidential and proprietary information being stored in an externalised network can be allayed. Perhaps the biggest advantage is the ability to transfer data from one site or platform to another. Other positive benefits include economies of scale, security and redundancy of data, with up-front capital expenditure rarely required, and CROs and sponsors alike paying for the space they need. There are potential challenges in terms of connecting all the different pieces of technology, and this will require data management systems to be carefully implemented.

**Mobile devices simplify data collection in real time**

This is an area that is starting to have a real impact in the clinical trials arena. First and foremost, mobile devices greatly simplify the collection of data in real time, but there are many other advantages that they offer. It is not unusual to see iPads used to collect patient data in a hospital setting, while mobile apps are increasingly being used to keep track of trials and approving documents. Their impact is only likely to grow as further functionality is added, for example the ability to capture data directly from clinical devices such as monitors and scanners.

**Regulatory Information Management (RIM) to satisfy regulatory demands**

The highly regulated nature of the pharmaceutical sector means it is vital for pharma companies to be in complete control of regulatory affairs data throughout the lifecycle of a product. There is a growing need for collaborative, integrated and effective global regulatory solutions in order to understand and meet the requirements of filing, timeliness and processes. This has led to a growing number of technology-driven regulatory solutions providers who cover areas such as electronic submission, tracking and management to keep up with the changing demands of the regulators.

**Medical communication essential to educate patients**

Pharmaceutical companies need to educate and inform their customers about the benefits and risks of their products, particularly new ones, based on clinical and economic data. This is referred to as medical communication. It is common for companies to outsource this work to MedComms agencies in a drive to save money while still delivering high quality documents. Services in this area include communication planning, publication planning, medical writing and stakeholder engagement.
Market outlook positive, underpinned by growing demand

Overall, the outlook for the CRO industry is positive, following a stabilisation after the first patent cliff that started in 2011 and the fact that drug pipelines are beginning to yield results. In addition, capacity has been reduced and pricing is gradually improving. A good outsourcing programme can help a pharma company reduce development costs by as much as 20–30%, according to Bank of America Merrill Lynch (BofAML), with the added advantage of providing expertise that will help sponsors navigate the long and complex drug approval process.

Reports from the large CROs themselves are buoyant. Quintiles, for example, claimed in its 2Q13 results presentation that there is a strong demand across all its customers, from small to large, and including biotech, with a 22% growth in net new business that quarter.

Outsourcing market expected to exceed $30b by 2018

According to estimates from BofAML, the overall annual market size of all the areas that could be outsourced to a CRO is about $90–95b. This represents about two-thirds of the worldwide R&D spend by the top 500 biopharma companies. In contrast, the current size of the CRO industry today is estimated at about $23–25b, which implies that only 24-28% of all the operations that could be outsourced to a CRO are, in fact, being outsourced. They estimate that this is poised to grow by 5–6% a year over the next five years, reaching $33b by 2018, reflecting a 30-35% penetration of the potential market with the potential to increase to more than 60% in the longer term. This is consistent with expectations for 5-8% industry growth recently voiced by Quintiles. Charles River Laboratories (CRL) expects to grow by 4–6% a year, while Covance estimates that it will continue to grow at around 7% a year, a figure it claims it frequently outperforms through gaining additional market share. For example, the company has indicated that it expects full-year revenue growth for 2013 of at least 9%.

Late-stage growing faster than early-stage

Demand for CROs is set to grow across early-stage development services such as preclinical and clinical pharmacology, as well as late-stage services such as Phase II-IV clinical trials and central lab services – albeit it at different rates (Chart 1).

The early-stage development space, with a potential market opportunity of $5.5-6.5b, remains difficult because of limited pricing power, according to BofAML, with drug sponsors continuing to favour investments in late-stage pipelines. While this leaves their analysts positive on the long-term promise of the early development market, they estimate that this segment will grow at a CAGR of 4% over the five years to 2018 as a result of on-going pressures. Covance claims Phase I capacity is still down, while Parexel says there has been little growth, although the market is starting to recover in the light of the improved funding environment for smaller companies.

Late-stage development, with an estimated market size of $15.5-16.5b, is growing more quickly, as pharma companies focus on investigational drugs in late-stage clinical trials, with fewer project delays and cancellations, and the higher volumes that benefit central lab operations. BofAML analysts project that, in contrast to the early-stage work, this segment of the market will grow at a CAGR of 7% in the next five years.

A highly concentrated market

The top 10 players account for more than 50% of the CRO market. However, this has been changing, with small and mid-sized players gradually increasing their market share over the past 10-15 years. This is probably a result of those CROs putting a greater focus on winning business from the biggest biopharma companies and signing long-term strategic growth agreements. Thus, there is a risk that smaller and medium-sized biopharma companies can feel under-served and overshadowed by their bigger competitors, leading them to favour smaller CROs over larger ones.

Emerging markets and Asia gaining importance

Conducting trials in ever-increasing numbers of countries is a necessary, and rapidly expanding, pursuit. The need to source growing numbers of patients for the very large Phase III trials that the regulators often demand is one factor, but countries such as China are also requiring studies to be done in their home markets if a new drug is to be approved there. Emerging markets offer large numbers of drug-naïve and diverse patients, who may be more likely to queue up to participate in a study rather than needing to be enticed.
However, the locations where trials are being done is shifting: CROs are seeing a drop-off in India, with somewhat improved conditions in China. In addition, there has been a rise in CRO services in Japan in the past year in response to a shortened regulatory application process.

**China benefiting from rising experience and improved quality standards**

R&D activities continue to grow in China, with both biopharma companies and CROs making big investments there. The traditional challenges of running clinical trials in China are becoming less of a problem, with the Association of Clinical Research Organizations working with government to provide shorter, more predictable timelines for approving clinical trials. Investigators and sites in China are becoming more experienced in running global trials, too, and meeting the quality requirements of international regulators. Companies such as AstraZeneca, Bayer, GlaxoSmithKline and Roche, who have set up large R&D centres in China, are creating even more opportunities for global CROs. Growing numbers of Chinese companies are also investing in pharma R&D as they look to expand from their base in the generic sector.

**India no longer an attractive location**

In contrast, there has been a dramatic drop-off in the number of clinical trials run in India, which will likely be down to under 100 in 2013 from a peak of about 500 in 2010. The regulatory requirements have changed, becoming more stringent and, in some cases, lengthening timelines. CROs and biopharma companies alike are playing catch-up. Clinical research has entered the political arena, and recent legal decisions have done little to allay the fears of western companies about IP protection and compulsory licensing. There are also worries about compensation rules for people injured by clinical trials. In the short term, the outlook is poor, and fewer companies are choosing to run trials in India.

**Japan slowly turning the corner**

Things are changing in Japan, too, but in a much more positive way. The historically slow and expensive drug approval process is starting to get faster, and new drug applications are on the rise. Large CROs are expanding their operations in the country; for example, Parexel now has four Japanese offices. Meanwhile, inVentiv entered into a strategic alliance with Japanese CRO Bell Medical Solutions to provide drug development services to companies running trials in Japan.

**CRO market participants: one-stop-shops vs. specialised players**

The players in the market can essentially be segmented into three groups according to size: top tier companies, mid-sized operations, and small, niche businesses. While common estimates put the number of companies active in the CRO sector at between 700 and 1,000, the top 10 account for the lion’s share of the market. Behind them comes a small group of mid-sized players offering more specialised services. These are followed by hundreds of niche players that have sprung up to cater to those small biotech and medtech companies who feel they do not receive adequate levels of service from the big players as they are too small to attract sufficient attention. Specialised, smaller outfits which provide innovative solutions or technologies are being snapped up by larger players who are looking to fill the gaps in their overall offering.

**Top tier players account for more than half the market**

The top 10 CROs by market share are listed in Table 4. Quintiles is, in revenue terms, the biggest company in the market, with 2012 revenues of $3.7b, making it substantially larger than the next biggest player, Covance, with revenues of $2.2b. PRA International joins this group following its recent merger with RPS.

**Table 4 Top tier global CROs**

<table>
<thead>
<tr>
<th>CRO</th>
<th>Estimated market share</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quintiles</td>
<td>15%</td>
</tr>
<tr>
<td>Covance</td>
<td>9%</td>
</tr>
<tr>
<td>Parexel</td>
<td>8%</td>
</tr>
<tr>
<td>PRA International</td>
<td>7-8%</td>
</tr>
<tr>
<td>Pharmaceutical Product Development (PPD)</td>
<td>6-7%</td>
</tr>
<tr>
<td>ICON</td>
<td>4-5%</td>
</tr>
<tr>
<td>inVentiv</td>
<td>2-4%</td>
</tr>
<tr>
<td>Charles River Laboratories (CRL)</td>
<td>2%</td>
</tr>
<tr>
<td>WuXi</td>
<td>2%</td>
</tr>
<tr>
<td>INC Research</td>
<td>2%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>52-62%</strong></td>
</tr>
</tbody>
</table>

Source: BofAML CRO Industry report, 2013; Credit Suisse CRO Industry report, 2013; Results Healthcare estimates

Leading players in the mid-sized segment are shown in Table 5.

**Table 5 Leading mid-sized CROs**

<table>
<thead>
<tr>
<th>CRO</th>
<th>Aptiv Solutions</th>
<th>Chiltern</th>
</tr>
</thead>
<tbody>
<tr>
<td>Accovion</td>
<td></td>
<td>MPI Research</td>
</tr>
<tr>
<td>ClinTex</td>
<td>MedPace</td>
<td>QPS</td>
</tr>
<tr>
<td>Novum Pharmaceutical Research Services</td>
<td>Premier Research</td>
<td>United BioSource Corporation</td>
</tr>
<tr>
<td>SynteractHCR</td>
<td>Theorem Clinical Research</td>
<td></td>
</tr>
<tr>
<td>WIL Research</td>
<td>Worldwide Clinical Trials</td>
<td></td>
</tr>
</tbody>
</table>
Biopharma R&D spend and outsourced share are the key growth drivers

As the previously discussed analyst data from BofAML suggest, the CRO market is growing at a healthy mid-single-digit rate. The two most important drivers behind CRO market growth are the increasing penetration of outsourcing, and rising biopharmaceutical R&D expenditure. These, in turn are influenced by global prescription sales, biotechnology financing, industry consolidation and broader economic head- and tailwinds.

Shift to more variable cost base drives increased outsourcing

Efficiency has never been more important, in light of the pressures pharma companies are facing from all directions. Patent expiries leading to generic competition and ever more stringent demands from regulators continue to have an impact on their bottom lines. However, after several years where spending on R&D was reduced, it is now rising again. For example, in their 2013 R&D Funding Forecast, Battelle and R&D Magazine say that they anticipate R&D spending will rise from $183b in 2012 to $189b in 2013. While this is a modest 3.3% increase, after years of decline and stagnation, it represents a step in the right direction for growth.

This expectation of growth is backed up by the ‘Strategic Partnerships 2013’ report from Parexel. In response to the question, ‘Do you expect your company’s outsourcing to increase, decrease or remain the same over the next five years?’, 65% or respondents said they thought it would increase, compared to 31% who anticipated it would remain the same, and just 4% who thought it would decrease.

Other big players in the CRO market also expect outsourcing to grow. Covance, for example, claims that many of its clients are a little more buoyant after navigating recent patent expiry issues, and believe the levels of outsourcing will continue to grow to 60% and more, with some companies already outsourcing most of their studies, and others just starting to go down that path. CRL, meanwhile, thinks that outsourcing may go up to as much as 75%, if not higher.

R&D spend expected to rise after two years of negative growth

R&D spend had been increasing year-on-year until the financial crisis began to bite. Total spend by PhRMA members decreased in four years out of five – in 2008, 2009, 2011 and 2012 (Chart 2). The negative effects of the global recession are being bolstered by mega-mergers and significant sales declines in the light of the patent cliff, with many big-selling drugs becoming available for generic competition. The cost of bringing a new drug to market continues to rise, with additional regulatory demands, trial complexity and cost of new technologies all having an impact. The Credit Suisse 2013 report puts the typical total cost at $1.2b, with a 57% increase in total procedures per trial, allied to a 64% increase in total investigative site work burden.

The expectation is that R&D spend is likely to increase again from 2013, albeit at a modest, low-single-digit rate. Analysis of EvaluatePharma consensus estimates presented in a 2013 industry report from Credit Suisse suggests a modest CAGR of 1.8% for R&D from 2012 to 2017. This report also forecasts that generics will represent about 88% of all US prescriptions towards the end of this decade, and thus a focus on innovation and maximising the potential of current pipelines will likely support some rebound in R&D investment.

Key growth drivers include:

- Most pharma companies are now past the patent cliff, with Credit Suisse forecasting 3-4% top-line growth in the next few years;
- The first half of 2013 has been one of the best IPO fundraising periods for biotech firms since 2004, according to data from the Wall Street Journal. In those first six months of the year, there had been 16 IPOs, raising nearly $1.2b. As of early October, there had been 20 biotech IPOs, compared to 19 IPOs in the whole of 2011 and 2012 combined;
- There is greater optimism about pharma pipelines, after a record number of FDA approvals in 2012. At 39, this is the highest number since the 53 approvals in 1996;
- Companies have largely recovered from the global financial crisis.
Current trends: focus on strategic alliances and adaptive trials

Perhaps the most important trends in the CRO market at the moment are strategic partnerships and adaptive trials.

**Strategic partnerships benefit sponsors and CROs alike**

With the growth in globalisation and collaborative research has come a desire within large biopharma companies to establish multi-year strategic partnerships with key suppliers who are able to assist across the entire spectrum of clinical trials. In order to satisfy these demands, CROs have to be big, global and offer a broad range of services. This has been fuelling consolidation in the sector, with smaller, niche players being snapped up by the CRO giants looking to expand their capabilities. As shown in Table 6, at least 20 major alliances have been forged in the past five years between the top tier CROs and large biopharma companies.

According to BoFAML, broadly speaking, traditional strategic deals offer sponsors attractive pricing alongside in-depth expertise in disease areas and regulatory compliance. In return, the CROs will secure a minimum level of work, improve backlog visibility, and gain exclusivity on certain products. They generally are the sole province of the big global players because of their geographic spread – particularly in emerging markets – and experience in multiple disease areas.

According to Parexel’s ‘Strategic Partnerships 2013’ report, this model is proving a success. It claims that 85% of client and non-client pharmaceutical executives surveyed believe strategic partnerships have had a positive impact on the client–CRO relationship. It identifies the major beneficial impact of the partnership to be a reduction in the level of client oversight that is required, with a higher percentage of costs being variable, and access to capabilities and expertise that are not available in house. This is supplemented by an improved global reach and accelerated time to market. These and other advantages are summarised in Table 7.

<table>
<thead>
<tr>
<th>Table 7 What’s in it for CROs and biopharma companies?</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CROs</strong></td>
</tr>
<tr>
<td>Improved visibility, allowing for long-term planning</td>
</tr>
<tr>
<td>Higher network utilisation</td>
</tr>
<tr>
<td>Opens doors for collaborations in other areas</td>
</tr>
<tr>
<td><strong>Large biopharmas</strong></td>
</tr>
<tr>
<td>Reduced level of required sponsor oversight</td>
</tr>
<tr>
<td>Reduced fixed costs/increases variable costs</td>
</tr>
<tr>
<td>Access to capabilities not found internally</td>
</tr>
<tr>
<td>Improved global reach</td>
</tr>
<tr>
<td>Accelerated time to market</td>
</tr>
<tr>
<td>Reduced overall development costs</td>
</tr>
</tbody>
</table>

Source: Parexel, ‘Strategic Partnerships 2013’; Results Healthcare research

**Table 6 Strategic alliances between large biopharma companies and CROs**

<table>
<thead>
<tr>
<th>Date</th>
<th>CRO</th>
<th>Biopharma</th>
<th>Location</th>
<th>Duration (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jul-13</td>
<td>Quintiles</td>
<td>Ascendancy Healthcare</td>
<td>China</td>
<td>2.5 (+2.5)</td>
</tr>
<tr>
<td>Jun-13</td>
<td>CRS</td>
<td>Bayer</td>
<td>Germany</td>
<td>n/a</td>
</tr>
<tr>
<td>May-13</td>
<td>Quintiles</td>
<td>Merck Serono</td>
<td>WW</td>
<td>n/a</td>
</tr>
<tr>
<td>Apr-13</td>
<td>Quintiles</td>
<td>BMS</td>
<td>WW</td>
<td>Multi-year</td>
</tr>
<tr>
<td>Apr-13</td>
<td>LabCorp</td>
<td>BMS</td>
<td>WW</td>
<td>5</td>
</tr>
<tr>
<td>Oct-12</td>
<td>Charles River</td>
<td>AstraZeneca</td>
<td>WW</td>
<td>5</td>
</tr>
<tr>
<td>May-12</td>
<td>Covance</td>
<td>Bayer</td>
<td>WW</td>
<td>n/a</td>
</tr>
<tr>
<td>Apr-12</td>
<td>PRA International</td>
<td>Amgen</td>
<td>WW</td>
<td>n/a</td>
</tr>
<tr>
<td>May-11</td>
<td>ICON/Parexel</td>
<td>Pfizer</td>
<td>WW</td>
<td>n/a</td>
</tr>
<tr>
<td>Mar-11</td>
<td>WuXi</td>
<td>BMS</td>
<td>China</td>
<td>5</td>
</tr>
<tr>
<td>Feb-11</td>
<td>Quintiles</td>
<td>Samsung</td>
<td>South Korea</td>
<td>n/a</td>
</tr>
<tr>
<td>Feb-11</td>
<td>PPD</td>
<td>Elan</td>
<td>WW</td>
<td>n/a</td>
</tr>
<tr>
<td>Feb-11</td>
<td>Covance/Quintiles</td>
<td>Takeda</td>
<td>WW</td>
<td>n/a</td>
</tr>
<tr>
<td>Jan-11</td>
<td>Parexel</td>
<td>Merck</td>
<td>WW</td>
<td>n/a</td>
</tr>
<tr>
<td>Sep-10</td>
<td>Covance</td>
<td>Sanofi</td>
<td>WW/France</td>
<td>n/a</td>
</tr>
<tr>
<td>Sep-10</td>
<td>Parexel</td>
<td>Eli Lilly</td>
<td>Asia Pacific</td>
<td>n/a</td>
</tr>
<tr>
<td>Sep-10</td>
<td>Parexel/PPD</td>
<td>GSK</td>
<td>WW</td>
<td>10</td>
</tr>
<tr>
<td>Jun-10</td>
<td>ICON/Parexel</td>
<td>BMS</td>
<td>WW</td>
<td>5</td>
</tr>
<tr>
<td>Oct-09</td>
<td>Quintiles</td>
<td>Eisai</td>
<td>WW</td>
<td>3</td>
</tr>
<tr>
<td>Aug-08</td>
<td>Covance</td>
<td>Eli Lilly</td>
<td>WW</td>
<td>n/a</td>
</tr>
</tbody>
</table>

Source: Company press releases
Other companies have also expressed positive remarks on the attraction of strategic partnerships. Quintiles, for example, believe that they lead to a higher utilisation of its whole organisation, which should bring benefits to its own bottom line in a competitive industry where there will always be pricing pressures. Meanwhile, CRL states that about a quarter of its total sales are now derived from strategic relationships, and Covance believes strategic partnerships have had a huge benefit for the company, with satisfied clients whose R&D costs have been lowered now looking to work with them in other areas such as market access.

**Adaptive trial design improves efficiencies and decision making**

Adopting adaptive trial designs increases the flexibility of clinical trials. They enable key parameters such as patient population, sample size and even dosing to be adjusted as the trial progresses, often in response to an interim analysis of safety and efficacy. An example is a futility analysis, which allows for a trial to be stopped early if there is a lack of efficacy, or greater efficacy than had been anticipated.

According to a report on Outsourcing-Pharma.com in June 2013, the adoption rate for adaptive trials has reached about 20%. A 2013 Tufts R&D senior leadership brief, meanwhile, suggests that futility-based early study terminations and sample size adjustments could save as much as $100–200m a year.

There are other advantages of adaptive trial designs. They can give a better understanding of the dose response profile, efficacy and safety while a project is still in Phase II, before progressing it to the larger – and hence more expensive – Phase III stage. It also encourages a seamless transition between different trials.

In response to the move towards adaptive trials, companies have emerged that focus on technologies to facilitate this, for example through the provision of software solutions, which presents another attractive acquisition niche for CROs.
M&A environment likely to remain dynamic

The M&A environment in the CRO space has been very active in recent years, with consolidation mainly occurring among the mid-sized and smaller players in the market, as they try to reach the critical mass they will need if they are to compete more effectively with the larger CROs. However, there have also been a number of bolt-on acquisitions by the larger players, who have been snapping up smaller firms to gain specific expertise they do not already have in house. Many CROs have been extending their services by expanding into areas of competence outside those traditionally offered, such as health economic outcome research, pharmacovigilance and market access. The fastest way to gain these skills and experience is by acquisition. There is also potential for large players in the clinical sector to expand their offering into earlier stage preclinical and discovery work, especially if sponsors start looking to outsource more of their R&D operations to a single supplier.

Consolidation in the CRO industry continues…

Many of the large CROs have expressed a desire to continue to expand their offerings by acquisition. Quintiles, for example, has said it will continue to scan for what we call tactical tuck-in acquisitions that enhance our capabilities to serve our clients. Parexel has said it has specific areas and conditions that companies need to meet in order to be attractive acquisition targets, most importantly that they must fit in with their strategy. While their footprint already covers most of the areas in which they want to be, there remain opportunities. CRL says it has seen many high-quality targets in terms of potential growth rates and quality of technology, with the potential to enhance geographic reach and add further capabilities. It added that the price expectations are often high because many are venture-owned, and they would only pay appropriate and rational prices for them. Covance, meanwhile, highlights the growth in M&A activity in the smaller to mid-sized companies, and funds being raised in the equity market.

…fuelled by both private equity and strategic buyers

The fundamental objective of strategic buyers in the CRO space is to build a comprehensive, global offering that allows for the management of large-scale, global, complex clinical trials. In addition, the aim is to reach critical mass, leaving the acquirer in a strong position to close strategic partnerships with biopharma companies.

The most important areas of focus include:

- Broaden clinical research services and expertise;
- Add services to improve certainty of product launch and reimbursement;
- Increase breadth of therapeutic capabilities;
- Build scale, particularly for late-stage capabilities;
- Increase geographic footprint;
- Expand customer portfolio, enabling valuable cross-selling opportunities;
- Acquire software solutions and expertise to build efficiencies.

There has been interest in this segment by private equity buyers for years. Here, the objectives are much more financially driven: to generate a high return on investment in the annualised 30% range, and achieve an exit within three to five years.

Key factors that render the CRO segment attractive to private equity buyers include:

- Attractive growth segment of the healthcare sector, with favourable macro-trends in life science R&D strategies, boding well for sustained high growth, capitalising on the outsourcing trend;
- High level of consolidation, given the highly fragmented nature of the industry;
- High visibility of revenues;
- Excess cash generation;
- Strong balance sheets;
- Limited exposure to regulatory and reimbursement risk, as well as healthcare reform.

The potential for a successful capital markets exit, as demonstrated by Quintiles’s recent IPO, presents an additional viable exit option. It is known from their filing in May of this year that PRA International had also explored this route prior to its acquisition by KKR in June. This can only have increased private equity interest in these businesses.
Overview of key deals in the space

Some of the most notable deals in the past few years include those briefly outlined below.

KKR acquired RPS from Warburg Pincus in July 2013, and merged it with PRA International, which it had acquired a month earlier as a secondary private equity transaction from Genstar. The combination of PRA and RPS creates what they claim to be fourth-largest contract research organisation, offering an enhanced array of services and capabilities to support its clients.

Parexel acquired market access service provider Heron in April 2013, following on from the acquisition of regulatory information management software provider Liquent in December 2012. The company claims these acquisitions are already having a positive impact on the company’s bottom line, and it continues to look for opportunities in those niches it does not already have covered.

Synteract bought Harrison Clinical Research (HCR) in March 2013. The acquisition was to form a new multinational top-tier CRO and will provide additional resources to support large, later phase programs.

Clinical Research Advantage, which is owned by Kinderhook Industries, bought Radiant Research, a Cincinnati-based site management and clinical research company, in November 2012. The acquisition will allow CRA to expand its geographic and therapeutic coverage, and Radiant to be the largest and most therapeutically diverse clinical trial site network in the US.

Charles River Laboratories acquired Accugenix in August 2012, and Vital River a few months later. The company says these acquisitions are a part of its drive to increase sales and gain market share, and that both acquisitions are performing above expectations. In particular, it describes Vital River as a timely addition to its portfolio as demand for high-quality research models in China is growing.

Hellman & Friedman LLC and the Carlyle Group bought Pharmaceutical Product Development (PPD) in October 2011. The resources from the two private equity groups will ensure that PPD gets an early mark on new drugs and allow PPD to have a more efficient drug approval process.

Medidata Solutions acquired Clinical Force, which provides software as a service (SaaS)-based clinical trial management systems for an undisclosed sum in June 2011.

INC Research bought Kendle International and Trident Clinical Research in May 2011. The strategic combination aimed to create a leading CRO to capitalise on drug development outsourcing trends.

Oracle acquired Phase Forward, which provides applications for life sciences companies and healthcare providers, in April 2010.

Table 8  Key deals in the CRO and related services space

<table>
<thead>
<tr>
<th>Date</th>
<th>Target</th>
<th>Target Type</th>
<th>Value ($m)</th>
<th>Buyer</th>
<th>Type of Buyer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sep-13</td>
<td>Stat-Tech Services</td>
<td>Clinical data services</td>
<td>--</td>
<td>CROS NT</td>
<td>CRO</td>
</tr>
<tr>
<td>Aug-13</td>
<td>Acurian</td>
<td>Clinical trial patient enrolment and retention services</td>
<td>--</td>
<td>PPD</td>
<td>CRO</td>
</tr>
<tr>
<td>Aug-13</td>
<td>Bracket</td>
<td>eClinical services</td>
<td>--</td>
<td>Parthenon Capital Partners</td>
<td>PE fund</td>
</tr>
<tr>
<td>Aug-13</td>
<td>Novella Clinical</td>
<td>Full service clinical CRO</td>
<td>--</td>
<td>Quintiles</td>
<td>CRO</td>
</tr>
<tr>
<td>Jul-13</td>
<td>Research Pharmaceutical Services (RPS)</td>
<td>Full service clinical CRO</td>
<td>1,300</td>
<td>KKR</td>
<td>PE fund</td>
</tr>
<tr>
<td>Jun-13</td>
<td>PRA</td>
<td>Full service clinical CRO</td>
<td>27</td>
<td>Charles River Laboratories</td>
<td>CRO</td>
</tr>
<tr>
<td>Apr-13</td>
<td>Heron</td>
<td>Evidence-based commercialisation services</td>
<td>123</td>
<td>JLL Partners</td>
<td>PE fund</td>
</tr>
<tr>
<td>Mar-13</td>
<td>ClinStar</td>
<td>Phase I-IV CRO</td>
<td>56</td>
<td>ICON</td>
<td>CRO</td>
</tr>
<tr>
<td>Mar-13</td>
<td>Harrison Clinical Research (HCR)</td>
<td>Full service clinical CRO</td>
<td>56</td>
<td>ICON</td>
<td>CRO</td>
</tr>
<tr>
<td>Feb-13</td>
<td>ClinForce, Assent &amp; AKOS</td>
<td>Clinical trial services, consulting and staffing</td>
<td>27</td>
<td>Charles River Laboratories</td>
<td>CRO</td>
</tr>
<tr>
<td>Jan-13</td>
<td>BioClinica &amp; CorLab Partners</td>
<td>Clinical trial services, consulting and staffing</td>
<td>123</td>
<td>JLL Partners</td>
<td>PE fund</td>
</tr>
<tr>
<td>Date</td>
<td>Target</td>
<td>Target Type</td>
<td>Value (Sm)</td>
<td>Buyer</td>
<td>Type of Buyer</td>
</tr>
<tr>
<td>--------</td>
<td>---------------------------------</td>
<td>------------------------------------------------------------</td>
<td>------------</td>
<td>------------------------------</td>
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</tr>
<tr>
<td>Dec-12</td>
<td>Liquent</td>
<td>Regulatory information management solutions</td>
<td>72</td>
<td>Parexel</td>
<td>CRO</td>
</tr>
<tr>
<td>Oct-12</td>
<td>Radiant Research</td>
<td>Study conduct, product development and patient recruitment services</td>
<td>--</td>
<td>Clinical Research Advantage (CRA)</td>
<td>CRO</td>
</tr>
<tr>
<td>Aug-12</td>
<td>Accugenix</td>
<td>Contract microbial identification testing</td>
<td>17</td>
<td>Charles River Laboratories</td>
<td>CRO</td>
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<tr>
<td>Aug-12</td>
<td>Drug Safety Alliance (DSA)</td>
<td>Safety and risk management services</td>
<td>28</td>
<td>United Drug</td>
<td>HC Services</td>
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<tr>
<td>Aug-12</td>
<td>Expression Analysis</td>
<td>Genomics testing and analysis services</td>
<td>--</td>
<td>Quintiles</td>
<td>CRO</td>
</tr>
<tr>
<td>Apr-12</td>
<td>eResearchTechnology</td>
<td>ePRO, cardiac safety and respiratory efficacy</td>
<td>400</td>
<td>Genstar Capital</td>
<td>PE fund</td>
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<tr>
<td>Feb-12</td>
<td>PriceSpective</td>
<td>Value strategy consulting</td>
<td>--</td>
<td>ICON</td>
<td>CRO</td>
</tr>
<tr>
<td>Feb-12</td>
<td>Skandynawskie Centrum Medyczne Sp</td>
<td>Polish clinical research company</td>
<td>--</td>
<td>Synexus</td>
<td>CRO</td>
</tr>
<tr>
<td>Jan-12</td>
<td>Nexus Oncology</td>
<td>Oncology clinical trials services</td>
<td>--</td>
<td>Ockham Development Group</td>
<td>CRO</td>
</tr>
<tr>
<td>Dec-11</td>
<td>BeijingWits Medical Consulting</td>
<td>Full service clinical CRO</td>
<td>16</td>
<td>ICON</td>
<td>CRO</td>
</tr>
<tr>
<td>Oct-11</td>
<td>Advion Bioanalytical Labs</td>
<td>Bioanalytical laboratory</td>
<td>--</td>
<td>Quintiles</td>
<td>CRO</td>
</tr>
<tr>
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<td>Aptiv Solutions</td>
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<td>Sep-11</td>
<td>Clinipace Worldwide</td>
<td>Technology-amplified CRO</td>
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Future prospects

M&A activity in the CRO space shows little sign of slowing down any time soon, with biopharmaceutical sponsors continuing to increase their outsourcing activities, whether small biotech or pharmaceutical giant, and right across the board from early stage research to late stage trials and post-marketing work. CROs, too, are experiencing continued growth in several areas, such as adaptive trials and programmes for personalised medicines and orphan drugs.

Other factors are also having an effect. Major shifts are being made in healthcare systems in attempts to reel in costs: a growing number of Phase III trials now include economic endpoints, and studies are carried out alongside the main trial to demonstrate cost effectiveness. These are not areas that biopharma companies of any size are likely to have deep experience in, and thus outsourcing services for outcomes research and comparative effectiveness research have intensified.

In turn, CROs themselves are having to put a greater focus – and spend more money – on regulatory compliance. Regulators such as FDA and EMA are adopting new guidance on safety, and there is a real regulatory push for electronic submissions and clinical trial data standards. These are all areas where CROs are looking to make acquisitions to bolster their capabilities.

The CRO support service market remains relatively fragmented and thus ripe for consolidation. For example, we believe CROs will look to acquire medical communication providers, health economics and outcomes research (HEOR) businesses, and companies offering pharmacovigilance services. There is also the potential for expansion into contract sales outsourcing, an area in which Quintiles is already active, but outsourcing rates in this sector currently remain low. With Quintiles filings estimated that this could be a $13bn addressable market, contract sales outsourcing has the potential to be the next hot area.

Strategic partnerships, too, are set to grow and evolve. While CROs will work to build new relationships with third-party players, they will also need to strengthen their ties among themselves, and also with pharma companies. Partnerships between CROs and pharma companies will continue to strengthen in certain areas, such as biosimilar development, personalised medicine and the companion diagnostics these require, orphan drugs and expansion into emerging markets.

Technology will remain an important focus for CROs, as the market continues to develop, innovate and adapt to meet the emerging needs of the pharma industry. For example, data management and IT activities will become ever more important, as companies look to speed up patient recruitment into trials and maximise participation.

There remains plenty of opportunity for consolidation within the CRO sector, particularly in the light of the ever-more competitive market environment for top and middle-tier CROs. Critical mass in terms of scale and global reach is likely to provide a key differentiation between CROs. In particular, more consolidation in Asian markets is likely, as CROs expand their activities in emerging markets to match the demands of their pharma company partners.

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About the authors

**Hemavli Bali**  
Executive Director, Results Healthcare  
hbali@resultsig.com  
+1 646 747 6506

Hemavli has spent over 14 years working in financial services and has almost 10 years of experience as a corporate finance specialist. She began her career in investment banks, working as a risk analyst at Nomura International plc and credit research analyst at Royal Bank of Canada Capital Markets. In Jan 2005, she joined Ernst & Young, where she worked in Transaction Advisory Services across a number of industry verticals, advising on corporate restructurings, mergers and acquisitions and performing valuation, business modelling and due diligence services. Hemavli joined Results International in 2008 and has recently relocated to New York to head up the firm’s Healthcare operations in North America as Executive Director.

Since joining Results, Hemavli has advised on a number of high-profile transactions, focused mainly in the healthcare sector.

Hemavli is a Chartered Accountant and holds a BSc in Economics from the London School of Economics. In her spare time she enjoys painting, dancing and squash. She is also a black belt in the martial art of Choi Kwang-do and danced in the London Olympics 2012 opening ceremony.

**Brigitte de Lima**  
PhD, CFA  
Results Healthcare  
bdelima@resultsig.com  
+44 (0) 20 7514 8255

Brigitte joined Results Healthcare in April 2013 from a long/short start-up investment fund focused on Healthcare. She has nine years of experience in the Healthcare sector, with particular expertise in Biotechnology. She combines a solid scientific background with strong financial forecasting and modelling, company analysis and equity valuation skills.

Brigitte started her career as a Healthcare Analyst at Datamonitor. She then worked as an Equity Research Analyst at Merrill Lynch and then Bank of America Merrill Lynch (“BofAML”) covering European Biotechnology, Mid cap pharma, Diagnostics and Life Science companies.

In 2011, Brigitte achieved top rankings in the two most prestigious investor surveys (Extel and Institutional Investor) in the Biotechnology category. While at BofAML, she launched coverage on a new sector (diagnostics) including three stocks and regularly published Biotech sector reports.

Brigitte has been a CFA Charterholder since 2009, holds a PhD in Virology from the University of Cambridge and obtained a first class Licentiate (equivalent to a Masters) in Biochemistry from the University of Lisbon, where she finished top in her year. She is fluent in German, Spanish and Portuguese and conversational in French.

In her spare time, Brigitte enjoys being active. She regularly participates in half-marathons, having finished in the top 1% of women in her first attempt in 2009, and competed in the London Triathlon (Olympic distance) in 2008-11. She also completed the Tour du Mont Blanc and the Alta Via 1 in the Dolomites.

**Carrie Yang**  
Senior Analyst, Results Healthcare  
cyang@resultsig.com  
+44 (0) 20 7514 8241

Carrie joined Results Healthcare in 2013. Prior to Results, Carrie was working for a venture backed healthcare IT company, Cambridge Healthcare, where she was responsible for fund raising, identifying and developing business opportunities.

Carrie started her career as a business analyst with a boutique financial services company, ZLNX Consulting Services China and was involved in a number of venture capital transactions. In 2007, she joined Fidelity Asia Ventures, the venture capital arm of Fidelity International, working across TMT, healthcare and life sciences sectors.

Carrie has an MA in corporate finance from Shanghai Economic and Finance University and an MPhil in Bioscience Enterprise from Cambridge University.

In her spare time, Carrie enjoys reading, drawing and playing badminton. She also loves travelling and exploring other cultures.
Acknowledgements

The White Paper has been prepared with contribution from Dr. Fran Brown. The deepest of thanks must be given to Dr. Brown for her willingness to give her time, knowledge, expertise and experience.

Fran Brown PhD
Senior Associate, Results International

Fran is a highly respected professional with proven leadership skills and 18 years broad experience within pharmaceutical development coupled with extensive hands on experience with all phases of drug development obtained in multiple geographical locations in North America and Europe. She possesses a broad knowledge of drug discovery and development principles and practice with a special focus on the needs associated with early projects.

After obtaining a degree in pharmacy and a subsequent PhD in pharmacokinetics Fran started her professional life in the clinical pharmacology department at Hoffman-La Roche. During her years at Roche she; was an integral part in the successful registration of two new products in global markets; worked as a clinical pharmacology liaison between research, development and business to align activities with long-term strategic business objectives; supported the scientific and commercial assessment of business development opportunities; led the strategic development of multiple compounds from pre-GLP toxicology to end of phase 2; held various management roles in both headquarter and affiliate sites including running a clinical operations group of more than 75 people.

Following a rich career at Roche, Fran joined Biovitrum (a Swedish biotech company) as Director of Clinical Operations. In her time there she built up a strong, experienced operations group, implemented data management systems and processes and established strong GCP awareness. She also, in conjunction with external service providers, put in place the global clinical, regulatory and pharmacovigilance infrastructure essential to support the commitments which come with the management of globally available products.