Capstone Headwaters

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BIO/PHARMA OUTSOURCED SERVICES

Institutional Industry Report

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JUNE 2018

INTRODUCTION

Over the past decade, the combined biotechnology, biopharma and pharmaceutical (Bio/Pharma) industry has been transformed by the growth of biopharma outsourced services (BPOS), which have become crucial in bringing new drugs to market. In fact, the BPOS industries are growing at about twice the rate of Bio/Pharma despite limited penetration of the addressable market opportunity.

BPOS firms don't own drugs or build product pipelines. They're not household names, with large ad budgets or rows of products lining drugstore shelves. But they are working behind the scenes, playing a critical role in nearly every aspect of drug development and manufacturing, e.g., screening potential drugs, managing clinical trials, designing manufacturing processes, providing packaging and distribution — and even handling sales and marketing. Moreover, as BPOS firms have increased the number of compounds under development, they have developed enhanced process and product expertise, widening their cost, operational and capital efficiency advantage over their Bio/Pharma customers.

Despite this rapid growth, BPOS remains a new industry in the early stages of development, as outsourced services still represent a small percentage of overall R&D and manufacturing spending. It is also highly fragmented, with hundreds of firms seeking to grow market share and add new capabilities. We expect this to lead to accelerated industry consolidation over the next few years, and to provide substantial opportunities for BPOS firms and their Bio/Pharma customers, as well as for private equity investors and public shareholders.

In the following pages, we look first at the structure of the BPOS industry and the main industry segments. We also discuss the current rate of spending on outsourced services and provide forecasts for market penetration and future growth. In the next section, we review the factors driving this growth, including consolidation, and highlight important M&A deals over the last year. We conclude with our industry outlook for 2018, and an appendix summarizing the recent performance of select BPOS stocks.

KEY MARKET SEGMENTS

The BPOS industry has two main segments, broadly defined as "contract research" and "contract manufacturing." Contract research organizations (CROs) provide outsourced R&D services and typically focus on drug development, from basic research and the testing of new molecules to the design and management of clinical trials and support services. By contrast, contract manufacturing organizations (CMOs) focus on the commercial production of drugs. Contract development and manufacturing organizations (CDMOs) represent a third, "hybrid" category of BPOS firms, and may provide both late-stage development services and manufacturing capabilities. In all, CROs, CMOs, and CDMOs provide their Bio/Pharma customers with a wide range of services, for example:

- molecular research and screening
- safety and toxicity testing
- clinical trial design and management
- small-scale production for clinical trials
- data analytics
- regulatory consulting and the preparation of new drug applications
- validation of manufacturing processes and quality assurance

Other subcategories in the BPOS space include site management organizations (SMOs), which manage clinical study sites for manufacturers, prepare and maintain case histories, and ensure proper institutional review; contract sales organizations (CSOs), which provide sales and marketing services; and contract commercial organizations (CCOs), which function as "turnkey suppliers" for comprehensive product launch and commercialization activities.

As shown in the table below, CMO and CDMO firms may also be grouped into "emerging" market segments based on their size, strategy and levels of scientific and developmental expertise. "Global Innovators," for example, may focus on complex, high-value products, while "Capacity-Driven" firms may specialize in the manufacturing of commodity drugs, generics, and OTC products. In yet another approach, CMO firms may be classified as "drug product manufacturers," which focus on the production of active pharmaceutical ingredients (APIs); and "dose manufacturers," which provide services ranging from formulation development to clinical and commercial-stage manufacturing; these services are necessary to produce finished drugs, which may contain a range of APIs.

We emphasize that these segment classifications (and their many acronyms), though useful for understanding the industry, are not strictly defined scientific or regulatory categories. BPOS firms often provide a mix of research, manufacturing, marketing and regulatory services that cut across segment boundaries. They are also continually adding new capabilities either through internal development or acquisitions. Most importantly, they are providing services that fill critical needs for their Bio/Pharma customers. These needs also represent a substantial — and rapidly growing — market opportunity for BPOS firms, which we examine in the next section.

EMERGING CMO SEGMENTATION

	Global Innovators	Niche Specialists	Capacity-Driven
Revenues	>$500M	$100M - $500M	$10M - $100M
Market Scope	Global (US, EU, Japan)	Home region, some global spillover	Home region
Strategy	High-value, complex products; innovative business models	New delivery of late lifecycle and generic drugs	Fill commodity capacity
Pharmaceutics Capabilities	Broad development tool box, range of primary dose forms, pre-formulation	Specialized formulation and delivery	Tech transfer and simple formulation
Regulatory Capabilities	Global registrations and QA	Global registrations and QA	Regional registrations and QA
Approvals/Portfolio	NMEs, new forms; few generics	NMEs, new forms; a few generics	Generics, OTC

Source: PharmSource, A GlobalData Company, 2017

BPOS MARKET SIZE AND GROWTH FORECAST

Estimating the size of the BPOS market isn't simple. Analysts may have different views of what counts as "outsourcing," and may exclude certain firms in their estimates. They will also inevitably apply different growth rate assumptions.

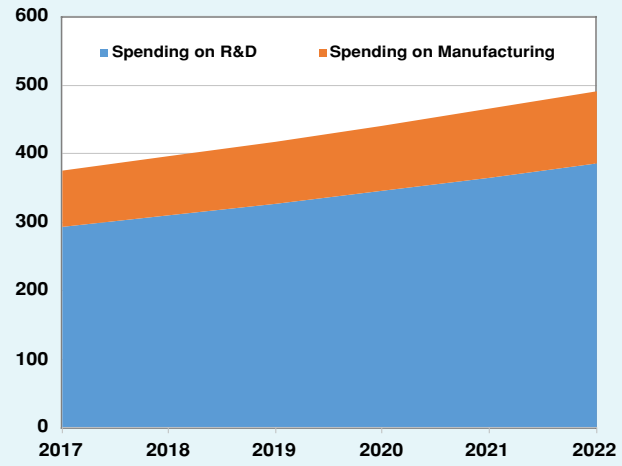
We take a straightforward approach to these calculations, beginning with current Bio/Pharma sales and then considering R&D and manufacturing spending as a percentage of such sales. In 2017, worldwide Bio/Pharma sales totaled $1.14 trillion, according to analysis from IQVIA. Based on estimates from ISR, industry R&D spending totaled $293.4 billion, or 25.7% of Bio/Pharma sales last year. Similarly, according to analysis from Results healthcare, manufacturing spending equaled approximately $80.9 billion, or 7.1% of 2017 Bio/Pharma sales. From this starting point, and assuming 5.6% compound annual growth in Bio/Pharma sales over the next five years, we estimate 2022 R&D spending of $385.3 billion and manufacturing spending of $106.2 billion. These forecasts are shown in the chart on the right.

Of course, these projections consider overall spending rather than the BPOS penetration rate — the amount of spending that is actually outsourced. We believe that the penetration rate is extremely low, though estimates vary based on the market segment and the specific services provided.

For example, market research firm Evaluate Pharma believes that approximately 28% of industry spending on development, formulation, and manufacturing was outsourced to BPOS companies in 2016, while Avid Bioservices, a CDMO firm, estimates that 26%-31% of this spending is currently outsourced. Similarly, ISR estimates that outsourcing accounted for 39.9% of the $85.9 billion spent on Phase 1 through Phase 4 clinical trials in 2017.

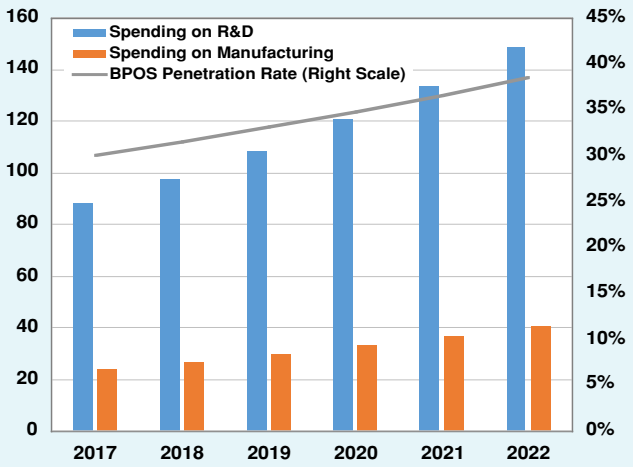
Based on these projections and our analysis, we estimate a 2017 BPOS penetration rate of 30%, implying overall spending of $88.0 billion on outsourced R&D services and $24.3 billion on outsourced manufacturing. However, we expect outsourcing spending to grow at an accelerated rate of 11% over the next five years, about twice as fast as overall research and manufacturing spending, with the caveat that growth will be faster in some areas than in others. Applying this 11% average growth forecast to our 2017 base-year estimates, we project spending of $148.3 billion on outsourced R&D and $40.9 billion on outsourced manufacturing in 2022, with a much higher penetration rate of 38.5%. These forecasts are summarized in the chart above.

BPOS MARKET SIZE ($ BILLIONS)



Sources: Argus Research, IQVIA, Inc., ISR, Results Healthcare, Capstone Headwaters

OUTSOURCED SPENDING TO BPOS ($ BILLIONS)



Sources: Argus Research, IQVIA, Inc., ISR, Evaluate Pharma, Avid Bioservices, Capstone Headwaters

We note that the expansion of outsourcing from adjacent markets, such as medical devices, could further boost these estimates. In all, we see a strong market opportunity for BPOS firms based on their current low penetration rate and ability to capture a greater proportion of R&D and manufacturing spending. We now take a closer look at the structural factors that are driving growth for outsourcing firms.

INDUSTRY GROWTH DRIVERS

The Bio/Pharma space is unique in that supply (new therapies) creates its own demand, i.e., patients/providers/payers respond to new treatments for previously untreated conditions in an inelastic way. The introduction of a new therapy that addresses an unmet need or that has higher efficacy or fewer side effects will itself generate strong demand that previously did not exist, or at least was not apparent. Consequently, Bio/Pharmas will set their R&D budgets based on expectations of future new drug approvals, i.e., additional supply (the lack of provable existing demand notwithstanding), and count on the resulting new demand and the creation of a larger addressable market. These expectations are driven by the ability of new therapies to drive changes in the therapeutic standard of care.

In addition, we note that the efforts of Bio/Pharma sponsors to add new labeled indications for existing drugs both increases overall development spending and shifts more spending to development from research. This phenomenon has materially increased, and will continue to increase, the portion of overall R&D spending per NME devoted to post-discovery clinical development.

In recent years, Bio/Pharma companies have pioneered the use of biologics and genetically based therapies, and launched groundbreaking treatments for cancer, hepatitis, HIV, and autoimmune diseases. These successes have led to strong sales and earnings for many Bio/Pharma firms, as well as soaring stock prices, with the S&P 500 biotech index rising 35% over the past year and 177% over the past five years.

COMPARATIVE RETURNS OF BIOTECH, PHARMA, S&P 500 HEALTH CARE, AND S&P 500 INDICES
(total return for periods ending June 11, 2018)

	1-year	3-year	5-year
SPDR S&P Biotech ETF (XBI) (based on the S&P Biotechnology Select Industry Index)	35.0%	21.5%	177.4%
iShares U.S. Pharmaceuticals ETF (IHE) (Large-cap U.S. pharma)	3.9%	-7.7%	63.5%
S&P 500 Health Care Index (includes pharma, biotech, health care services, insurance and distributors)	12.0%	20.0%	92.5%
S&P 500 Index	16.8%	41.5%	91.5%

However, high returns also mean high risks, as once-promising products may fail clinical trials and send stock prices plunging. Bio/Pharma firms also operate in a capital-intensive industry, with high development costs, long lead times, and intense competition. To sustain margins, they must maintain and build market share for their products and quickly replenish their pipelines as older drugs come off patent. BPOS firms help them to meet these challenges — and increase the potential returns of drug development — by allowing them to lower costs and allocate capital efficiently.

CRO firms may, for example, have expertise in developing specific types of products, such as oncology or immunology drugs, and be able to carry out this work more quickly and at a lower cost than the Bio/Pharma customer. They may also have employees with the skills needed to complete the development of a particular drug, or expertise in preparing and managing new drug applications in different international markets. This may be particularly helpful for smaller firms that lack the experience to move product candidates through clinical trials and regulatory review.

Similarly, CMO and CDMO firms may have special expertise in the design and validation of manufacturing processes, or in the technology needed to manufacture biologic drugs. They may also be specialists in "single-use" systems, in which drugs are manufactured in facilities that utilize disposable components unique to each protocol. These systems reduce the use of water and energy, lower the risk of cross-contamination, and eliminate the need to remove and clean/calibrate re-useable components. They also greatly reduce the need for employees with specialized skills who may be difficult to hire and retain and eliminate a material source of compliance risk.

Other cost savings may be generated through "insourcing," in which employees of a BPOS firm are integrated into the day-to-day operations of the customer company and provide their services on the customer's premises. Insourcing reduces the chance of data exchange errors between the customer and the BPOS provider since all work is carried out on the customer's systems, and allows production issues to be resolved in real time. It also enables the customer to realize the efficiencies of outsourcing while maintaining control of in-house activity and leveraging its existing investment in facilities and equipment. While insourcing requires flexible employees and compatible corporate cultures, it often costs customers less per full-time employee than traditional off-premise outsourcing.

INDUSTRY GROWTH DRIVERS (CONTINUED)

BPOS companies may also help customers to allocate capital efficiently by enabling them to match their manufacturing capacity to actual needs — in short, by rightsizing their manufacturing footprint. Rather than constructing a new plant, for example, Bio/Pharma firms may find it more efficient to outsource manufacturing to CMOs, especially in the case of biologics that require specialized equipment, and other drugs with narrow target markets and high per-unit production costs. This approach reduces the cost of unused capacity as products come off patent or if demand for a product slows. It may also provide a way for smaller firms to retain and commercialize their intellectual property.

The increasing ability of drug researchers to identify highly specific biomarkers and disease pathways is reflected in the rapid disappearance of broad-spectrum therapies intended for large patient populations, along with their concomitant multibillion-dollar markets. In their place have come narrower indications and a greater number of less ubiquitous associated therapies with much smaller patient populations. However, the development timelines and costs for these narrow-spectrum therapies remain largely the same as for their blockbuster predecessors. The result is a rapidly evolving market model for new therapies, with an increased level of clinical research activity needed to support the replenishment of the drug pipeline. The economics of this evolution clearly favor the fastest and most cost-efficient drug development programs – a key factor driving growth in the BPOS industry.

GROWTH THROUGH CONSOLIDATION

While BPOS has transformed drug development and manufacturing, the BPOS industry is itself undergoing rapid transformation and consolidation. In some cases, traditional Bio/Pharma firms (such as Johnson & Johnson) are reconfiguring their manufacturing capacity in response to changing needs. They may, for example, sell basic production capacity to BPOS firms even as they purchase capacity in other areas, such as biologics, where in-house resources are lacking. Other firms may decide to enter the BPOS space by adding new platforms and business lines, as scientific instrument manufacturer Thermo Fisher did with its recent acquisition of Patheon.

Meanwhile, established outsourcers may merge with other BPOS firms in order to add scale or acquire additional capabilities. This trend has been accelerated by customer companies themselves, which often prefer to work with a smaller number of large outsourcers — or a single outsourcer — which can provide a broad range of services. Working with fewer providers also helps customers to speed development time, reduce delays, and strengthen quality assurance. In all, we expect a range of factors, at both customers and BPOS vendors, to drive consolidation in the still highly fragmented BPOS industry. We review several recent deals below.

NOTABLE DEALS IN 2017-2018

M&A activity in the BPOS space accelerated in 2017, with 67 deals, up from 42 in 2016. The disclosed dollar volume of transactions rose to $54.9 billion from $31.4 billion. The pace of consolidation has slowed somewhat in 2018, but is still robust. Key deals included:

Medidata/SHYFT. Medidata continued to extend the use of informatics to drive efficiencies in clinical research through its $195 million acquisition of SHYFT. The acquisition has enabled the further automation of the drug research, development and approval process.

Recipharm/Evotec/Sanofi. Continuing the trend of Bio/Pharma sponsors (see also, Roche) divesting manufacturing facilities to adapt facility investment to costs/needs, Sanofi sold its contract inhalation drug business and manufacturing center to Recipharm for $72.2 million, and its infectious disease unit to Evotec for $69.6 million plus an earnout of up to $12 million; Recipharm and Evotec have used this method to significantly expand its capacity footprint in Europe.

Madison Dearborn Partners/Alcami. MDP, a $23 billion AUM alternative asset manager, acquired Alcami, a mid-market CMO, for an undisclosed amount after a robust private auction that drew bids from multiple P/E firms and other financial buyers.

WuXi Apptec IPO. WuXi AppTec raised $353 million in an IPO at a valuation of in excess of $35 billion on the Shanghai Stock Exchange after having been taken public and private within the past three years. Its subsidiaries WuXi Biologics and WuXi NextCode went public at a valuation of more than $500 million, and was taken private, respectively, both in 2017.

FujiFilm/JSTG Holdings/Irvine Scientific Sales/IS Japan. FujiFilm acquired JSTG Holdings, Irvine Scientific Sales and IS Japan for a combined $800 million in a series of transactions squarely aimed at creating a major provider of cell culture media to support cell therapy and stem cell therapy Bio/Pharma sponsors.

Charles River/MPI Research. Charles River continued to amass scale and additional pre-clinical research tools and capacity through its $800 million acquisition of MPI Research. We note that Charles River has made 11 acquisitions since 2013 at an aggregate valuation of approximately $2 billion.

Thermo Fisher Scientific/Patheon. Clearly bullish about the BPOS industry, Thermo Fisher paid $7.2 billion to acquire Patheon, one of the largest CDMOs, as a platform for consolidating other CDMO assets. We note that Patheon went public in 2016 at a much lower valuation of $3.0 billion.

Avantor/VWR. Avantor, a global supplier of ultra-high-purity materials for life science applications backed by P/E firm New Mountain Capital, acquired VWR, a provider of product, supply-chain and service solutions for laboratory and production customers. VWR had been owned by a group of private equity firms.

INC Research/inVentiv. INC Research and inVentiv merged in a $7.4 billion deal to create a larger CRO, now called Syneos Health. Syneos also has a contract commercial business that provides customers with consulting, sales, and communications services on an outsourced basis.

Lonza/Capsugel. To add dose manufacturing capacity, Lonza acquired Capsugel in a deal valued at $5.5 billion. Lonza was already a leader in hard capsule technologies and API manufacturing. In April 2018, Lonza added biologics capacity by opening what it described as the world's largest cell- and gene-therapy manufacturing facility.

Pamplona Asset Management/Parexel. Highlighting interest from financial buyers in the CRO space, Parexel was acquired by Pamplona for $5.0 billion in September 2017. Pamplona outbid ICON plc, one of the industry's best-capitalized CROs.

Avid Bioservices/Peregrine Pharmaceuticals. One of the more notable transactions of the year was not an M&A deal but a corporate restructuring. Previously a division of Peregrine Pharmaceuticals, Avid Bioservices emerged as a separate business after Peregrine sold the rights to an oncology drug that Avid had been developing. The separation was driven by activist shareholders. Avid now focuses exclusively on developing and manufacturing biologics for third-party customers. These services include cell-line development and the commercial biomanufacturing of large molecules such as monoclonal antibodies and recombinant proteins.

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NOTABLE DEALS IN 2017-2018 (CONTINUED)

PRA Health Sciences/Symphony Health. PRA Health Sciences acquired Symphony for its healthcare data and analytics capabilities. The $530 million acquisition will help PRA to differentiate itself in the highly competitive contract research space.

IMS Health/Quintiles/IQVIA. The PRA Health acquisition follows the 2016 combination of IMS Health, a data and analytics firm, with Quintiles, a CRO, to create IQVIA. Again highlighting the importance of data analytics, the combined company is able to leverage IMS's extensive data on patients with specific illnesses to recruit the right patients for clinical trials.

Please see the Appendix at the end of this report, where we provide a broader list of BPOS M&A transactions for the period 2017-2018. As the table shows, the annual number of transactions has increased substantially in recent years.

2018 INDUSTRY OUTLOOK

We expect continued growth in the BPOS industry in the near term as clinical programs expand and the pace of new drug approvals picks up. We note that the FDA approved 46 new molecular entities (NMEs) in 2017, a 20-year high, as well as 12 biologics — matching the record set in 2015. We are particularly encouraged by the increased focus on biologics and biosimilars. These drugs appeal to Bio/Pharma companies because of their high sales (think Humira and Enbrel), but also provide opportunities for BPOS firms due to their high development costs and need for specialized manufacturing facilities. Biosimilars may be an especially strong area for BPOS firms over the next two years given the small number of these drugs on the U.S. market and the FDA's efforts to promote price competition in the biologic/biosimilar space and expand patient access to biosimilars.

BPOS providers may also benefit as Bio/Pharma firms' savings from a lower U.S. tax rate, along with repatriated foreign earnings, provide resources for additional R&D and manufacturing spending.

As discussed above, we expect further consolidation in the industry as Bio/Pharma customers seek to work with a smaller number of suppliers, and as BPOS firms add scale and expand their capabilities. These could include new capabilities in drug dosing or formulation, gene therapy technologies, the analysis of clinical trials, or outsourced sales and marketing services. Based on these factors and the estimated penetration and growth rates provided above, we look for 2018 CRO revenue of $75.5 billion and CMO/CDMO revenue of $37.7 billion, up 11% from 2017.

STOCKS ON THE MOVE IN THE BPOS SECTOR

Illumina (ILMN) is launching new high-end and mid-range gene sequencers. ILMN's instruments and assays are used in drug discovery and in the identification of appropriate population segments for specialized treatments, such as immuno-oncology. ILMN is generating strong revenue growth from instrument placements, consumables, and assays.

Bio-Techne (TECH) is seeing strong demand for its proprietary systems and consumables for protein analysis as well as for diagnostics products.

An increase in its contract backlog should drive future revenue for Medpace Holdings (MEDP), a global full-service CRO. New business awards rose 36% to $128.2 million in the most recent quarter, faster than revenue growth. The EBITDA margin also rose.

Siegfried Holdings (SFZN), based in Switzerland, is expanding production capacity with the acquisition of a drug product manufacturing facility from Arena Pharmaceuticals.

ICON plc, one of the world's largest CROs, is seeing strong market demand for its services as its backlog and new contract awards rise faster than revenue.

Lab Corp. (LH) rose on the news of the renewal of a large contract with UnitedHealthcare and the signing of a new contract with Aetna.
On the downside, Eurofins (ERF) saw a sharp drop in its stock price after posting disappointing revenue growth in 1Q18.

BPOS STOCKS ON THE MOVE
(year-to-date returns)

Name	Ticker	Price Change	Total Return
Illumina	ILMN	28.41%	28.41%
Bio-Techne	TECH	23.11%	23.65%
Medpace Holdings	MEDP	21.70%	21.70%
Siegfried Holdings	SFZN	20.54%	21.37%
ICON Plc	ICLR	19.09%	19.09%
Lab Corp.	LH	16.71%	16.71%
Thermos Fisher	TMO	14.36%	14.45%
Evotech AG	EVT	9.70%	9.70%
IQVIA Holdings	IQV	6.77%	6.77%
SGS SA	SGSN	1.48%	4.69%
Charles River Labs	CRL	4.11%	4.11%
Lonza Group	LONN	1.79%	2.85%
Syneos Health	SYNH	-1.32%	-1.32%
Catalent	CTLT	-2.46%	-2.46%
PRA Health	PRAH	-3.71%	-3.71%
Cambrex	CBM	-3.96%	-3.96%
Eurofins Scientific	**ERF**	**-16.75%**	**-16.75%**

Source: Bloomberg

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APPENDIX

Capstone Headwaters Life Sciences Global BPOS Transaction Summary

January 1, 2017, to date

Transaction Date	Acquired/Investee	Acquiror/Investor	Valuation ($ in 000s)	Acquired Industry Space
6/18/18	Sanofi infections disease unit	Evotec	$69,610	R&D CRO
6/13/18	Sanofi contract inhalation drug business and manufacturing ctr	Recipharm	$72,200	CMO
6/13/18	MetaSafe AB	Admescope	Not Disclosed	CRO
6/12/18	SHYFT	Medidata	$195,000	Real-world evidence
6/11/18	Sciformix	Labcorp/Covance	Not Disclosed	CRO
6/4/18	Alcami	Madison Dearborn Partners	Not Disclosed	CDMO
5/30/18	Cynata Therapeutics	Fidelity International	$5,200	CDMO
5/15/18	Unknown	PolarityTE	Not Disclosed	CRO
5/8/18	WuXi AppTec	IPO	$353,233	CRO/CDMO
5/3/18	Rapid Micro Biosystems	Bain Capital, Xeraya Capital, Ashahi Kasei Medical, Longitude Capital, Quaker Partners, TVM Capital, Richard K. Mellon & Sons	$60,000	Microbial detection technology
5/2/18	Genohm	Agilent Technologies, Inc.	Not Disclosed	Laboratory LIMS and ELN systems
5/1/18	Total Scientific	RxCelerate	Not Disclosed	CRO
4/26/18	ADC Biotech	Downing	$1,600	Antibody-drug conjugate (ATC) contract services
4/23/18	Kalexsyn, Inc.	Dipharma Francis S.r.l.	Not Disclosed	CRO - chemistry
4/23/18	PSC Biotech cGMP aseptic fill finish manufacturing facility	Lyophilization Services of New England (LSNE)	Not Disclosed	CDMO
4/18/18	Analytica Laser	Certara	Not Disclosed	Real-world evidence
4/12/18	Biocytogen	Series C equity investment	$65,000	CRO
4/10/18	PathoQuest	Charles River	Not Disclosed	NGS Sequencing
4/5/18	JSTG Holdings; Irvine Scientific Sales; IS Japan	Fujifilm	$800,000	Cell culture media
4/5/18	CMAB Biopharma	CD Capital; C-Bridge Capital, Cormorant, Quianhai FoF, Tigermed	$34,000	CDMO
4/3/18	Hilbert Paradox	Genae	Not Disclosed	Health data management; data equity firm.
3/16/18	Continuum Clinical	Worldwide Clinical Trials	Not Disclosed	Real-world evidence
3/15/18	Solvo Biotechnology	CiToxLAB	Not Disclosed	Non-clinical CRO
2/26/18	Proximagen U.K. Operations	BenevolentAI	Not Disclosed	AI drug discovery research IT
2/13/18	MPI Research	Charles River	$800,000	CRO
2/1/18	Partner Therapeutics	Perceptive Advisors, Adams Street Partners, MidCap Financial	$60,000	CMO
1/25/18	XtalPi	Sequoia China, Google, Tencent	$15,000	AI clinical research IT
1/18/18	Pisgah Labs	Ipca Laboratories	$9,650	CMO/API manufacturer
1/16/18	MKS Research	Optimapharma	Not Disclosed	CRO
1/15/18	KWS BioTest	Charles River	$20,000	CRO
1/9/18	Ranbaxy Malaysia	Sun Pharmaceuticals	$4,500	Table-making JV
1/4/18	Nitin Lifesicences	Recipharm	$53,000	CDMO
1/1/18	DNAnexus	Foresite Capital, Microsoft, GV, WuXi Next CODE	$58,000	Clinical research IT
1/1/18	BaseCase	Certara	Not Disclosed	Life sciences data visualization software-as-a-service
12/21/17	Wolfe Laboratories	Pace Analytical Services	Not Disclosed	CRO
12/20/17	Crown Biosciences	JSR Life Sciences/KBI Biopharma	$400,000	CRO
12/13/17	Eurotrials	CTI Clinical Trial	Not Disclosed	CRO
11/15/17	Pharmaterials	Quotient Sciences	Not Disclosed	CDMO
11/6/17	Aquila BioMedical	Concept Life Sciences	Not Disclosed	CRO
11/6/17	MDDX Research & Informatics	Bioclinica	Not Disclosed	Clinical research IT
11/1/17	Milestone Research Organization	CRO Factory	Not Disclosed	CRO

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APPENDIX (CONTINUED)

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January 1, 2017, to date

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9/29/17	PSR Group BV	Ergomed	$8,550	Orphan drug CRO
9/29/17	PSR Group BV	Ergomed	$5,700	CRO
9/20/17	Roche small-molecule manufacturing plant	Recipharm	Not Disclosed	CDMO
9/19/17	Cook Pharmica	Catalent	$950,000	Biologics CDMO
9/18/17	EAG Laboratories	Eurofins Scientific	$780,000	Laboratories
9/14/17	Quantum Pharma	Clinigen	$225,000	Specialty pharma
9/13/17	Antidote	Series B equity investment	$11,000	CRO
9/7/17	Therapure Biomanufacturing	3SBio JV w/ CPE Funds	$290,000	CDMO
9/7/17	Teckro	Series B equity investment	$10,000	CRO
8/31/17	Syncom	Mercachem	Not Disclosed	Drug discovery
8/31/17	CNIM Group/Bertin Technologies/Bertin Pharma	Amatsisgroup	Not Disclosed	Laboratories
8/31/17	CNIM Group/Bertin Technologies/Bertin Pharma	Ocodesign Group	Not Disclosed	CRO
8/29/17	Viroclinics	Parcom Capital	Not Disclosed	CRO
8/24/17	Envigo	Avista Healthcare (to become Envigo International Holdings)	$924,000	Non-clinical CRO
8/17/17	vivoPharm	Cancer Genetics	$12,000	CRO
8/10/17	eConsent technology, ConsentNow, Patent Genesis	WIRB-Copernicus Group	Not Disclosed	CRO
8/10/17	Symphony Health Solutions	PRA Health Sciences	$530,000	CRO
8/10/17	Brains On-Line	Charles River	$21,000	CRO
8/3/17	Mapi	ICON	Not Disclosed	CRO
7/31/17	Chiltern	Labcorp/Covance	$1,200,000	CRO
7/30/17	Aptuit	Evotec AG	$300,000	CRO
7/24/17	Advinus Therapeutics	Eurofins	Not Disclosed	CRO
7/10/17	Amatsigroup	Eurofins	$150,000	CDMO
7/7/17	Capsugel	Lonza	$5,500,000	Contract capsule manufacturer CMO
7/6/17	NextPharma Technologies	CapVest	Not Disclosed	CDMO
7/5/17	Science Exchange	Norwest Venture Partners, Maverick Capital Ventures, Union Square Ventures, Collaborative Fund, Index Ventures, OATV, the YC Continuity Fund and others	$28,000	Outsourced research services provider CRO
6/28/17	Censo Biotechnologies	Collaboration with Evotec	Not Disclosed	CRO
6/21/17	Parexel	Pamplona Capital Management LLP	$5,000,000	CRO
6/14/17	Selexis SA	JSR Life Sciences/KBI Biopharma	Not Disclosed	Cell line developer CDMO
6/13/17	Alphora Research, Inc.	Eurofins Scientific	Not Disclosed	API CDMO (drug ingredient manufacturing and testing)
6/13/17	WuXi Biologics	IPO - HKEX	$511,000	Biologics R&D
6/6/17	Albany Molecular Research, Inc.	Carlyle/GTCR	$922,000	CDMO
6/1/17	Eurofins	Public bond offering	$760,000	CRO
6/1/17	WuXi AppTec	IPO	$3,300,000	Pharmaceutical discovery, genome testing and immunotherapy development, precision medicine
5/16/17	Patheon	Thermo Fisher	$7,200,000	CDMO
5/10/17	inVentiv Health, Inc.	INC Research Holdings, Inc.	$7,400,000	CRO/CDMO
5/5/17	VWR International	Avantor	$6,400,000	CRO supply chain
5/4/17	CRO division of Vector Oncology	George Clinical (Sydney, Australia)	Not Disclosed	Oncology clinical trials
5/2/17	WuXi AppTec - WuXi NextCode	Temasek (lead); Yunfeng Capital (Jack Ma) (lead); Amgen Ventures; 3W Partners (China)	$75,000	Genomic information; precision medicine
5/1/17	PharmaCell	Lonza	Not Disclosed	Gene and Cell CMO
5/1/17	STA	PRC OTC market offering	$2,270,000	API CDMO

(continued on next page)

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APPENDIX (CONTINUED)

Capstone Headwaters Life Sciences Global BPOS Transaction Summary

January 1, 2017, to date

Transaction Date	Acquired/Investee	Acquiror/Investor	Valuation ($ in 000s)	Acquired Industry Space
4/26/17	Metrion Biosciences	Venomtech	Not Disclosed	Ion channel modulators
4/25/17	Science 37	Glynn Capital Management; GV (Google Ventures); Amgen Ventures; Lux Capital; Redmile Group; dRx Capital (Qualcomm/Novartis investment JV; Sanofi Genzymes BioVentures	$29,000	Patient recruitment CRO
4/19/17	Mytrus	Medidata	Not Disclosed	Clinical trial patient informed consent software/IT CRO
4/14/17	Chiltern	Labcorp/Covance	$1,300,000	CRO
3/27/17	Lyophilization Services of New England (LSNE)	Permira Funds	Not Disclosed	Lyophilization services
3/14/17	TransCell Science	BioreclamationIVT	Not Disclosed	Cell-based assays for phenotypic screening CRO
3/1/17	Concept Life Sciences	Metrion Biosciences	Not Disclosed	Discovery CRO
3/1/17	Shin Nippon Biomedical Laboratories Clinical Pharmacology Ctr	Pharmaron	Not Disclosed	CRO
2/19/17	Assay.Works	Metrion Biosciences	Not Disclosed	Discovery CRO
2/15/17	PRA Health	Takeda	$4,100	CRO
2/14/17	QS Pharma/CRL	Quotient Clinical	Not Disclosed	GMP CDMO
2/8/17	SeaView Research	Quotient Clinical	Not Disclosed	Phase I CRO
2/2/17	The Medical Affairs Company	Parexel	Not Disclosed	Full-service contract medical organization/Medical affairs specialist (MSL)
1/23/17	HD Biosciences	WuXi AppTec	Not Disclosed	Biology-focused preclinical drug discovery contract research organization (CRO)
1/12/17	Xceleron	Pharmaron	Not Disclosed	MS specialist
1/9/17	Eternygen	Epidarex Capital; Evotec; Founds Technologie/IBB Beteiligungsgesellschaft; 2 family offices	$8,460	Metabolic diseases
1/4/17	New Iberia Research Center	Crown Bioscience	$1,000	Pre-clinical non-human primate models
1/1/17	Integrated Development Associates Co. Ltd.	Chiltern	Not Disclosed	CRO
1/1/17	CMC Biologics	AGC Asahi Glass	Not Disclosed	CDMO
1/1/17	InterHealth Nutriceuticals	Lonza	$300,000	Nutritional ingredients maker

GLOSSARY

SUBSETS OF BPOS
The is no specific regulatory structure for BPOS, so the criteria for description are informal and frequently blurred, particularly by firms that operate in more than one of the described spaces. However, a basic and generally accepted taxonomy of BPOS has emerged by description along the continuum from immediate post-candidate discovery through manufacture and distribution of finished drug product and post-approval regulatory consultation. Some of those basic divisions are described below:

CROs – Contract Research Organizations
A contract research organization (CRO) that provides support to the pharmaceutical, biotechnology, and biopharma industries in the form of research services outsourced on a contract basis. A CRO may provide such services as biopharmaceutical development, biologic assay development, commercialization, preclinical research, clinical research, clinical trials management, and pharmacovigilance. CROs range from large, international full-service organizations to small, niche specialty groups. CROs that specialize in clinical-trials services are often referred to as Clinical Research Organizations, contributing further to the acronym infestation. These CROs offer Bio/Pharma clients the expertise of managing the development of a new drug compound from its conception to FDA/EMA marketing approval[4], without the drug sponsor having to maintain a staff for these services.

CMOs – Contract Manufacturing Organizations
A contract manufacturing organization (CMO) offers manufacturing services, with volume capabilities ranging from small amounts for preclinical R&D to larger volumes necessary for clinical trials (Phases I-IV) purposes and long-term, industrialized production for commercialization.

CDMOs – Contract Development/Manufacturing Organizations
A contract development and manufacturing organization (CDMO) offers both contract drug development and manufacturing services. Comprehensive services range from early-stage R&D services such as synthesis, scale-up, formulation development, stability studies and method development through to manufacturing services as a CMO.

SMOs – [Clinical Research] Site Management Organizations
A site management organization (SMO) assumes, as an independent contractor with the clinical investigator, one or more of the regulatory obligations of a clinical investigator, e.g., preparation and maintenance of case histories, ensuring compliance with IRB review, and/or manages clinical study sites on behalf of the sponsor and/or drug manufacturer.

CSOs – Contract Sales Organizations
A contract sales organization (CSO) provides an outsourcing sales/marketing team for one or a group of products for a sponsor in order to realize decreased costs, efficient operations and reduced risks.

CCOs – Contract Commercialization Organization
A contract commercialization organization (CCO) provides, on a turnkey basis, the services and activities necessary to launch and commercialize a new drug (e.g., inVentive Health, which has helped develop or commercialize 81% of novel new drugs approved by the FDA and 70% of those approved by the EMA, in the past five years).

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