Capstone Headwaters

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WHAT IS PAST IS PROLOGUE: THE REPRISE OF OUTSOURCING

Institutional Industry Report

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EXECUTIVE SUMMARY

The well-managed, nonopportunistic use of outsourcing to support drug development and, in particular, the development and manufacturing functions, allows sponsor-innovators to take advantage of specialist expertise, resulting in higher compliance and productivity levels, shorter turnaround and set-up times, access to difficult-to-find expertise, shorter completion dates, and lower overall costs.

In past reports, we have highlighted the accelerating rationalization of the bio-/pharma outsourcing sector. This phenomenon is evidenced by the increasing presence of outsourcing firms in multiple functions along the drug development path, from early-stage research consulting support through multiple modalities of preclinical development (in silico, multiple animal models, etc.), to functions in the clinic (trial design, patient recruitment, clinical supplies development and manufacture, trial site hosting and management, data capture and analysis), and on to reporting and regulatory consulting, commercial manufacture, packaging, sales/marketing, and distribution.

Each of these outsourced activities has unique characteristics, but all have proliferated for similar reasons. Each represents an opportunity for a pharma, biopharma, biotech or cell/gene therapy sponsor-innovator to address multiple strategic objectives. Primary among those objectives are to (i) bring a higher level of expertise and efficiency to bear on each outsourced functional step than could likely be applied by an in-house department, (ii) rationalize the allocation of capital by reducing/eliminating investment in functions whose output can be obtained from third-party vendors, and (iii) reduce overall drug development costs by engaging outsource service providers at pricing that compares favorably with the cost of performing the same functions internally. Outsourcing enables a sponsor-innovator to accelerate the completion of a drug development program while increasing efficiency and quality. For the sponsor-innovator, it frees substantial capital from investment in fixed assets, underutilized personnel and processes that involve high regulatory and execution risk. This capital can be used for the creation/acquisition of IP that can form the basis of new products or product families that can, in turn, increase the operational leverage of the existing capital base.

One might ask whether drug sponsor-innovators are (or should be) divesting manufacturing capacity because they (i) choose to redeploy capital toward drug development, or (ii) believe outsourcing reduces the cost and accelerates the timeline of bringing products to market while also improving quality and regulatory compliance. In our view, the answer in both cases is a resounding "YES." Both are compelling reasons to increase the outsourcing of development and manufacturing processes to CDMO/CMOs, and each has a demonstrable effect on the overall profitability and quality/compliance results of the sponsoring company.

A real-world example of this confluence of effects is the recently announced (and vigorously debated) acquisition of Celgene (CELG) by Bristol-Myers Squibb (BMY). In its public statements, BMY has set a high bar for cost synergies in connection with the transaction. The high-profile debate over the financial merits of the deal assures that the combined entity's ability to meet that bar will be closely monitored. We believe that Bristol-Myers plans to divest some Celgene manufacturing facilities in order to reduce any manufacturing overlaps between the two companies. (BMY is targeting $2.5 billion in annual run-rate cost synergies by the third year following the closing. It expects to achieve 10% of these savings by leveraging Bristol's biologics footprint and through procurement efficiencies.) We assume that in order to achieve the promised effects on operating margins, the post-transaction BMY will need to liberate the capital invested in these facilities and redeploy it to the development of a wider array of new drugs. We expect this to be the strategic course, even if the immediately observable effect is to apply such amounts to reduce debt and thereafter use the resulting borrowing capacity to fund an increased drug development budget.

Michael Ewing

Redeployment of Capital

It is difficult for most of us to imagine a time when Big Pharma housed all of the support functions necessary to execute a new post-discovery drug development program, though it was true once. The redeployment of the capital previously allocated to these functions has been driven by the increasing levels of expertise and efficiency available from third-party vendors when compared with in-house departments. As the complexity and diversity of the processes required to execute a drug development program have increased, the availability of properly educated/trained/experienced personnel has declined, even as their cost has significantly increased. Likewise, the number and diversity of the testing processes needed to complete such a program have greatly expanded, making it increasingly challenging and costly to maintain such expertise in house. The result is a frequent mismatch between the capabilities available in house and those required in any given drug development protocol, leading to a steady decline in the ability to rely on in-house resources and significant increases in their (predominantly fixed) costs. This has led to the poor utilization of capital resources allocated to drug development, resulting in higher per unit costs and a lower return on invested capital.

We foresee capital allocation analysis replicating itself within individual sponsor-innovators both in the context of (i) regular internal strategic analysis of operating cost reduction opportunities and returns on invested capital, and (ii) post-transaction capital deployment rationalizations. One can be forgiven for asking if such a trend will mean a glut of manufacturing capacity up for sale (and whether we are in a buyers' or sellers' market). We believe that the liquidation of manufacturing capacity and the redeployment of the freed capital to other purposes (primarily expanded drug development programs) will not affect the overall supply/demand balance. Sponsor-innovators will still need development and manufacturing capacity for the same programs, the ownership of the facilities notwithstanding. Further, the increased cash available as a consequence of (i) reduced development and manufacturing operating costs, plus (ii) the capital freed through the sale of redundant development and production capacity, will be available for redeployment to additional drug programs, resulting in an ever-greater number of such programs being in progress at any given time.

This phenomenon has particular relevance to cell/gene therapy because, as we have previously noted, that sector is transitioning from a long period of research & development focus to an emphasis on regulatory approvals and commercialization. To illustrate the trend, a summary of cell/gene therapy sector statistics from 2018 reveals that:

- The FDA approved 206 investigational new drug applications, twice as many as in 2017.
- Companies working in various aspects of the regenerative medicine market (including gene and gene-modified cell therapy, cell therapy, and tissue engineering) raised a total of $13.3bn in financing, mostly through venture capital and follow-on public offerings.
- Just over $20bn was spent up front on regenerative medicine acquisitions [See Endnote 1].

Specifically, with respect to the cell/gene therapy sector, it's worth remembering that, far from there being a "glut" of manufacturing capacity, the manufacturing needs and current manufacturing capacity for cell/gene therapies point to a worsening "capacity crunch." Published reports have estimated that the current capacity shortfall in the cell/gene therapy space is 5x or 500%, i.e., five times the current capacity would be in use if it were available [See Endnote 2]. Further, BioPlan expects the shortfall to increase to 50x or 5,000% in five years, implying that 50x current capacity would then be needed [See Endnote 3]. Any potential for a temporary oversupply of manufacturing capacity in other sectors of the bio/pharma space should be quickly corrected as suppliers of outsourced services shift capability across specialties. In short, as the need for additional manufacturing capacity in the sector accelerates, the already identified shortfalls will become ever more acute. The response must be an increased dedication of capital to the creation of de novo manufacturing capacity and the conversion of existing capacity in adjacent technologies to meet the ballooning needs of the cell/gene therapy sector.

Nonclinical Contract Research

Over the past two months, two major CROs, Charles River Laboratories and Covance, a subsidiary of LabCorp, have made acquisitions to bolster their capabilities in nonclinical contract research services. In February, Charles River agreed to acquire Citoxlab, a nonclinical CRO specializing in regulated safety assessment services, nonregulated discovery services, and medical device testing, with operations in Europe and North America. In April, LabCorp. said that it would acquire the nonclinical CRO services business of Envigo. The deal will expand the nonclinical drug development capabilities of LabCorp's Covance unit.

These two transactions, in a discrete space and coming, as they have, in quick succession, lead us to ask: Are these deals signs that CROs see the nonclinical side of research services as more fragmented than the clinical side and thus ripe for consolidation? Or are they evidence that CROs want to strengthen relationships with biotech and drug developers in order to expand into earlier stage research activities? We will see the answers in the next few months.

The Effects of Biosimilars and "Biobetters"

We have observed a tendency to consider biosimilars and so-called "biobetters" together when discussing the effect of each on outsourcing trends. While it is true that they both target existing biologic products and seek to lever the scientific and regulatory success those target products have achieved, the strategic and development considerations attending them are very different. A biosimilar is intended to be as nearly as possible a duplicate of

the in-market target biologic product in a way that is analogous to generic versions of small-molecule drugs. However, the biologic origins of biosimilars make it impossible to achieve the exact equivalence seen in generics. Therefore, additional clinical studies are typically required to demonstrate that the unavoidable differences in manufacturing and output of the biosimilar product do not materially change the mechanism of action and the efficacy of the original therapy. These additional clinical studies are typically not sufficiently burdensome that they negate the economic advantages sought, but neither are they trivial.

Biobetters, however, while similarly levering the mechanism of action and regulatory success of the target biologic, seek to improve on the performance of the original innovator protein by enhancing activity, reducing dosing, or minimizing deleterious side effects. For example, Amgen's Neulasta is an improved version of Neupogen, permitting a reduced dosing schedule. Biobetters allow sponsors to reduce the risk of developing a wholly new product by levering the established mechanism, safety and efficacy profile of a target biologic. The result, however, is a materially different molecule than that of the target therapy. As such, the FDA requires that all of the clinical trials and associated regulatory steps that would be required of a wholly new biological therapy be completed for the biobetter. The development costs of the biobetter are thus essentially the same as those for a new biological product, but with significantly greater chances of successful registration. This is likely to result in a drug inventory for a given biobetter sponsor-innovator that is less costly to bring to market owing to the many fewer failed programs.

There are thus compelling reasons of cost sensitivity to believe that both biosimilar and biobetter sponsors will increasingly outsource the development and manufacture of their products to CDMOs and CMOs. The same factors (narrow margins requiring heightened focus on manufacturing costs and efficiencies) that have driven generic pharmaceutical companies to outsourcing apply equally to biosimilars. Similarly, for the same reason that sponsor-innovators of de novo biologics are gravitating to outsourcing, and in order to improve regulatory success rates and ensure development and production capacity, sponsors of biobetters will increasingly use outsourcing to access highly capable providers of these essential services. Kate Hammeke, VP of Industry Standard Research (ISR), the lead author of a report entitled "Biosimilars Manufacturing: Key Considerations and Expected Outsourcing Practices" [See Endnote 4] has said: "My suspicion is that all the different approaches used in the small molecule space between generics and the originator product will be tried in the biosimilar space." She also expects the industry to increasingly focus on biobetters rather than biosimilars ". . . because improving upon an existing biologic offers an opportunity to be compensated for the cost of developing the 'better' aspect." [See Endnote 5]

The materially narrower margins of biosimilar/biobetter manufacturers relative to those of their de novo biologics brethren make the efficiencies available from outsourcing essential to profitability. This sentiment was expressed as far back as 2011 by Hans Engels, president and business unit director of DSM Pharmaceuticals Inc.: "The rise of various forms of biosimilars (follow on biologics, biobetters) is inevitable. From a business perspective we must be aggressive in entering this field of play to satisfy our fiduciary responsibility to shareholders. And from an ethical perspective we want to be a significant player in providing low-cost, high-quality products to patients."

Outsourcing Drivers

Multiple factors induce (indeed, require) drug sponsor-innovators to continue to increase their reliance on outsourcing providers throughout the R&D and manufacturing process. They include:

Diverse expertise

As the industry's understanding of the mechanisms of disease and the effectiveness of potential therapies has grown, so, too, has the range of expertise required to execute and support the development, manufacturing, testing and compliance processes required to register a drug. The growing range and complexity of the competencies necessary to perform this work requires sponsor-innovators to perform "make-or-buy" analyses at two levels: (i) whether they can acquire and maintain the highly sophisticated capability necessary to perform such work in-house, and (ii) whether it is cost effective, both on a per program basis and overall, to do so. In most cases, the wide range of capabilities required argues against maintaining them in house.

Shortage of expertise; need to amortize across industry

The expansion and escalating complexity of the expertise required to support drug development carries with it a concomitant growth in the sheer numbers of persons and overall capability required. The result has been a significant and growing shortage of qualified personnel to perform such functions, whomever their employers are. It has become impractical for any single drug sponsor-innovator, regardless of its scale, to acquire, train and retain such personnel for deployment only on its own drug development projects. Through outsourcing, however, such capabilities can be positioned and deployed across multiple specialty firms. The cost of these capabilities can also be "amortized" across multiple development efforts for diverse sponsor-innovators.

Start-up/transition cost/delay

A significant driver of in-house drug development costs is the transition from project to project in terms of set-up, initial training and project initiation, and associated "dead time." Single- or narrow-expertise contractors, by their nature, are able to transition from one project to another more quickly and cost-effectively than

in-house departments, which are frequently embarking on a given development task, in the precise form required, for the first time.

Conversion of fixed costs to variable operating costs

The fixed cost of the human and infrastructure assets required to support a given drug development function can be significant, particularly if it involves substantial employee training or certification costs or regulatory processes. Similarly, maintaining in-house development staff across multiple functions imposes significant fixed costs on sponsor-innovators, which may be recoverable only on a limited and intermittent basis. The ability to eliminate many fixed costs in favor of variable, project-specific costs (for projects that are actively progressing) represents a significant cost-saving opportunity for sponsor-innovators.

Increased expertise and efficiency of third-party vendors

Third-party drug development vendors limit their work to one or a limited number of adjacent, relatively narrow bands of specialization in which they can develop and maintain a high level of operating expertise and efficiency. This keeps costs low (and boosts profitability), while also enabling sponsor-innovators to realize more timely and higher quality results than would be possible with an in-house strategy at a reduced cost. In short, outsourcing vendors enable a multitude of drug development functions to be initiated sooner, and performed more quickly and cheaply, with significantly higher regulatory compliance and less distraction for management, than similar in-house development.

Past is Prologue

The discrete disciplines of biopharmaceuticals in general and cell/gene therapies in particular have begun to emerge from decades of basic science development and experimentation to clinical study, and, more recently, to therapeutic use. As with traditional pharmaceuticals and even biotechs, these newer therapeutics have experienced, and will continue to experience, lengthy and costly research and development gestations as their novel mechanisms of action and challenging clinical profiles extend and complicate development. However, unlike typical pharmaceutical products, cell/gene therapies carry with them a costly and complex "manufacturing" protocol, particularly in the case of autologous therapies that take a "personalized medicine" approach. The laboratory and other processes necessary to create a therapeutic cell/gene therapy typically require highly skilled technicians and highly complex, costly processes and equipment to produce dosages for patients.

Thus, the factors that have driven pharmaceutical sponsor-innovators to consistently increase the portion of post-research development and manufacturing activity carried out by outsource providers have precise parallels in the biopharmaceutical and cell/gene therapy sectors. Moreover, these parallels arise at an even earlier point in the evolution of these therapies from development projects to commercial products. The key determining factors include industry-wide shortages of appropriately trained and experienced personnel, low utilization of in-house capabilities, high capital investment requirements, the opportunity for shortened development timeframes, tighter regulatory compliance, and higher rates of successful development and registration.

Therefore, we expect (and are seeing signs of) a rate of adoption of the outsourcing model for biopharmaceuticals and cell/gene therapies that generally follows the curve (albeit more steeply) that has historically applied to the pharmaceutical industry. In fact, the incentives to outsource (cost, complexity, the need for and shortage of qualified personnel, competitive pressures, and small market sizes -- including a "market of one" for autologous therapies) are significantly greater for biopharmaceuticals and cell/gene therapies than for traditional pharmaceuticals. We thus expect the transition from in-house to outsourced development and manufacturing to be more pronounced and accelerated compared to the observed pattern for the pharmaceutical industry.

Oddly enough, the segment that is most likely to see a high degree of outsourcing is the one that is currently seeing the least, i.e., gene/cell therapy. In clinical and early-stage commercial development and manufacturing, sponsor-innovators often believe that they alone are capable of doing the work properly; however, the expense and episodic nature of this work provide a very strong incentive to turn to outsourcing providers as volumes increase and their well-trained and costly workforce becomes ever more nomadic. We further anticipate that significantly higher per-unit costs (and proportionately higher gains in efficiency) as well as requirements for significantly greater expertise and more exact manufacturing execution will accelerate this trend.

Real Market Evidence

To date, there are only four cell/gene therapy products approved for marketing in the U.S. However, even at this early stage, several recent transactions demonstrate that sponsor-innovators of these therapies will benefit from conducting significant portions, or perhaps all, of their drug development and manufacturing activity through outsourced vendors. This can be illustrated by the M&A market's active reshuffling of the deck in the cell/gene therapy development and manufacturing sector. A survey of selected transactions, presented in the table below, shows how the real allocators of capital (i.e., company managements and shareholders) believe such capital should be deployed (see table on following pages).

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Hitachi Chemical Advanced Therapeutics Solutions, LLC/Hitachi Chemical Regenerative Medicine – Caladrius Biosciences/PCT	Hitachi acquired the cell therapy development and manufacturing business (PCT) of Caladrius for US$75M in a two-step transaction completed in 2017. Caladrius's stated intention was to deploy the funds received from the PCT sale to support Phase II development of its lead type 1 diabetes candidate, T-regulatory cell mediated tumor cell/dendritic cell technologies for autoimmune and cardiology indications, and a cell therapy project focusing on critical limb ischemia, as well as to identify new pipeline candidates. "Hitachi Chemical's purchase of our remaining interest in PCT unlocks the value of this asset for our Company both by transforming Caladrius into a well-capitalized pure play therapeutics development company and by eliminating our need to contribute the tens of millions of dollars of future capital investment in PCT needed for it to fully realize its cell therapy commercial manufacturing growth goals," said David J. Mazzo, Ph.D., Caladrius CEO, upon completion of the transaction. "The transaction provides considerable nondilutive capital to fund the execution of our ongoing Phase II trial while also allowing us to exploit compelling therapeutic prospects." A pitch-perfect example of the redeployment of capital from in-house development resources to investment in other drug development projects that we believe is a harbinger of the evolution of this sector.
Fujifilm – Biogen	Biogen sold Denmark Manufacturing ApS, a subsidiary engaged in biologics manufacturing in Denmark, to Fujifilm Corp. in March for $890M. The transaction included the continued employment of the subsidiary's approximately 800 employees and a manufacturing services agreement with a minimum purchase commitment guarantee, among other terms. Along with its sale of Denmark Manufacturing ApS, Biogen announced that it would acquire Nightstar Therapeutics, a UK-based gene therapy company focused on adeno-associated virus (AAV) treatments for inherited retinal disorders, for approximately US$800M. Coincidence? We believe not.
Fujifilm – Irvine Scientifics Sales Company, Inc., and IS JAPAN CO., LTD	Fujifilm acquired these sister companies from JXTG Holdings in 2018 for approximately US$800M. The companies are cGMP manufacturers and distributors of cell culture media used in the growth and proliferation of cells, essential to R&D and manufacturing of biopharmaceuticals and regenerative therapies. Quoting from the Fujifilm press release: *To advance its growth strategies in the healthcare area, Fujifilm continues to invest in contract development and manufacturing of biopharmaceuticals and regenerative medicine. . . . With the acquisition of ISUS and ISJ, Fujifilm will now be able to provide a broad product portfolio from biopharmaceuticals to in vitro fertilization and cell therapy, strengthening its global business. Utilizing [the] . . . cell preparation and culturing technologies of its group companies . . . Fujifilm will accelerate the development of highly competitive cell culture media, supporting the further growth of its cell culture media business. Further, by combining the Fujifilm Group's bio-medical-related technologies and products with the cell culture media technologies and products of ISUS and ISJ, the company will maximize the synergies in areas other than the cell culture media business as well. The expected synergies are 1) the further expansion of the contract development and manufacturing business for biopharmaceuticals, 2) the acceleration of research and development in the area of regenerative medicine, and 3) the further expansion of the reagent business.*
Catalent – Cook Pharmica	Catalent acquired Cook Pharmica, an integrated provider of drug substance and drug product manufacturing and related services, including clinical or commercial cell culture manufacturing, in October 2017 for US$950M. The acquisition will strengthen Catalent's position as a leader in the rapidly growing areas of biologics development and analytical services, manufacturing, and finished product supply. The proceeds from the transaction will provide further capital for Cook Group's other businesses, including Cook Biotech, a developer and manufacturer of products for tissue repair and regenerative medicine applications utilizing its proprietary extracellular matrix (ECM) technologies and processes.

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Therapure – 3S Bio; IPO	Therapure Biopharma Inc. is a Canadian company with three divisions, (i) a biologics-focused CDMO with cGMP manufacturing capability, (ii) a research and development platform, and (iii) a plasma protein rare disease therapeutic creator of new drugs. In September 2017, a joint venture of 3SBio Inc., a major Chinese biopharmaceutical company, and CITIC Private Equity, a PRC-owned private equity firm, agreed to acquire Therapure's CDMO division for US$290M and make additional investments in Therapure's other businesses. In March 2018, Therapure's biologics division filed a registration statement with the SEC for an IPO. In May 2018, 3SBio terminated its plan to acquire the Therapure CDMO for undisclosed reasons. The upshot of this activity is that, though its plans have been at least temporarily frustrated, Therapure clearly intended to liquidate its outsourcing business and retain its therapeutic operations, albeit in a public structure to which it would be free to apply the proceeds of the CDMO sale as additional capital investment, i.e., a redeployment of capital.
Fujifilm – Merck BioManufacturing Network	Fujifilm acquired Diosynth, Avecia and MDS Biologics, together comprising the Merck BioManufacturing Network (MBN), from Merck for US$490M in 2011. The transaction included a commitment from Fujifilm to continue to provide manufacturing services to MBN's legacy customers and simultaneously represented (i) Fujifilm's rapid and aggressive move into biologics contract manufacturing (it was the fifth of nine such transactions to date), and (ii) Merck's desire to shed legacy manufacturing capacity acquired during its acquisition of Schering-Plough in order to devote capital and management focus to its core drug development activities. Merck spokesman Ian McConnell said the sale was part of Merck's ". . . ongoing effort to focus on core competencies. [Our] commitment to developing biologics and biosimilar products remains unchanged."
AstraZeneca – Novartis/AveXis	AstraZeneca sold a six-building cell/gene therapy manufacturing campus for scaling, manufacturing and testing gene therapies that it had previously shut down to the AveXis gene/cell therapy CDMO subsidiary of Novartis. No better example could be imagined to illustrate the divergent strategies being deployed by even the largest pharmaceutical manufacturers and their cell/gene therapy subsidiaries. It should be noted, however, that AstraZeneca has, of late, focused its cell and gene therapy initiatives on collaborations with small innovators in the space. It is likely, therefore, that its needs for meaningful development and manufacturing capacity are likely far in the future, further strengthening the incentive to liquidate its investment in cell and gene therapy manufacturing capacity and redeploying those assets in new drug development projects via collaboration and otherwise.
Charles River – Citoxlab	Citoxlab announced in February that it would be acquired by Charles River Laboratories for approximately US$510M. Citoxlab is a nonclinical contract research organization (CRO) specializing in regulated safety assessment services, nonregulated discovery services, and medical device testing. With operations in Europe and North America, the proposed acquisition of Citoxlab would further strengthen Charles River's position as the leading early-stage CRO by expanding its scientific portfolio and geographic footprint. This should enhance the company's ability to partner with clients across the drug discovery and development continuum.
Fujifilm – Cellular Dynamics	Cellular Dynamics, located in Madison, Wisconsin, was sold for US$307M in cash to Fujifilm in April 2015. CDI manufactures living human cells on an industrial scale and to precise specifications. This process is based on induced pluripotent stem cells and involves taking tissue from donors, returning the donor cells to an embryonic-like state, and then directing them to turn into desired cell types such as neurons and heart, liver, and retinal cells. The technology has applications in drug discovery and screening, toxicity testing, cell banking, and the development of experimental cell-based therapies that could in theory heal or regrow body parts.

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Danaher – GE Bio-processing	GE announced in February that it would sell its BioPharma business to Danaher for approximately US$21.4 billion, including US$21 billion in cash. The BioPharma unit manufactures equipment and special resins that help pharmaceutical companies to discover and mass produce biopharmaceuticals like Humira, Remicade and Rituxan, which are designed to fight autoimmune diseases such as rheumatoid arthritis and psoriasis. It is also helping vaccine developers and researchers explore immunotherapy. GE is expected to use the net proceeds of the transaction to pay down debt, while Danaher will immediately become a significant supplier of tools for drug R&D.
Hitachi Chemical Advanced Therapeutics Solutions, LLC/ Hitachi Chemical Regenerative Medicine – apceth Biopharma GmbH	Hitachi announced in January that it would acquire apceth, a GMP contract manufacturing organization specializing in cell and gene therapy. apceth is a leading CDMO in Advanced Therapy Medicinal Products in Europe, the world's second largest cell/gene therapy market following the U.S. It provides multiple cell therapy products for clinical and commercial use. It has comprehensive expertise in GMP manufacturing of autologous and allogeneic cell types that are either native or genetically modified. It also has substantial experience with various cell products, including mesenchymal stem cells (MSCs), hematopoietic stem cells (HSC), lymphocytes, monocytes, dendritic cells, cord blood derived stem cells, and has the potential to expand to CAR-T and induced pluripotent stem cell (iPSC) technologies
Fujifilm – Japan Tissue Engineering Co.	Fuji acquired Japan Tissue Engineering Co., a pioneering provider of tissue-engineered regenerative medical materials in 2010 for US$88M. JTE formed the base for Fujifilm's entry into the cell/gene therapy CDMO segment in combination with the expertise acquired from its chemical business.

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APPENDIX

Capstone Headwaters Life Sciences Global BPOS Transaction Summary

January 1, 2019, to date

Transaction Date	Acquired/Investee	Acquiror/Investor	Transaction Value ($ in 000s)	Acquired Industry Space
04/18/19	Envigo	Labcorp/Covance	Not Disclosed	CRO; research products
04/15/19	Paragon Bioservices, Inc.	Catalent	$1,200,000	Viral vector development and manufactuing CDMO
04/11/19	Asklepios BioPharmaceutical	TPG Capital; Vida Ventures	$225,000	Developer and manufacturer of AAV
04/09/19	Avectas	Seamus Mulligan and others	$10,000	Biomanufacturing-in-a-box
04/03/19	CiVentiChem U.S. Operations	Sterling Pharma Solutions	Not Disclosed	API manufacture
04/02/19	Finger Lakes Clinical Resaerch	Evolution Research Group	Not Disclosed	Clinical trials site
04/02/19	Astero Bio Corporation	BioLife Solutions	$8,000	Cell and gene therapies tools
04/02/19	AstraZeneca manufacturing facilities	AveXis/Novartis	Not Disclosed	Biologic drug manufacturing facilities
04/01/19	Precision BioSciences	IPO	$145,400	Gene-editing technology
03/26/19	Saama Technologies	Perceptive Advisors	$40,000	AI data analytics
03/24/19	Brammer Bio	Thermo Fisher	$1,700,000	Viral vectors for gene and cell therapies
03/20/19	Ovation.io	Madrona Venture Group; Borealis Ventures, Nat Turner; Zac Weinbert, StagedotO; David Shaw	$5,000	Provider of cloud-based lab information systems
03/12/19	Biogen	Fujifilm	$890,000	Biologics manufacturing facilities & supply contract
03/06/19	Beam Therapeutics	Redmile Group, Cormorant Asset Management, Google Ventures, Altitude Life Science Ventures, F-Prime Capital, ARCH Venture Partners, Eight Roads Ventures, Omega Funds	$135,000	Next-gen CRISPR gene editing technologies, base editing programs

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APPENDIX (CONTINUED)

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January 1, 2019, to date

Transaction Date	Acquired/Investee	Acquiror/Investor	Transaction Value ($ in 000s)	Acquired Industry Space
03/04/19	Xellia Pharmaceuticals	Nichi-Iko/Sagent Pharmaceuticals	Not Disclosed	Small molecule and biologics manufacturing site & supply contract
03/04/19	Hesperix S.A.	Xenetic	Not Disclosed	XCART platform technology
02/28/19	MolecularMD	Icon	Not Disclosed	Molecular diagnostic specialty lab
02/15/19	Chiron Behring Vaccines	Bharat Biotech	Not Disclosed	Manufacture of rabies vaccine Rabipur
02/14/19	Culture Biosciences	Section 32; Refactor Capital; Verily	$5,500	Biomanufacturing CMO
02/13/19	CiToxLab	Charles River	$510,000	Preclinical services
02/13/19	Velocity Clincial Research	Undisclosed	$20,000	Patient recruitment CRO
02/13/19	Argos Therapeutics	SCM Life Sciences; Genexine	$11,100	Stem cell manufacturing
02/12/19	Azedra	Progenics	$8,000	Radiopharmaceutical manufacturing facililty
02/07/19	Aetion	Sanori, Horizon Health Services, UCB, McKesson	$63,000	Real-world data software
02/06/19	Simbec-Orion	CBPE Capital	Not Disclosed	CRO
01/31/19	Velos eResearch	WIRB-Copernicus Group	Not Disclosed	Clinical trial management solutions
01/31/19	Apceth Biopharma	Hitachi Chemical Advanced Therapeutics Solutions	$86,800	Cell and gene therapy CMO
01/31/19	Publicis Healthcare Solutions	Altamont Capital Partners	Not Disclosed	CCO
01/09/19	Boston Biomedical Associates	Factory-CRO Group	Not Disclosed	CRO
01/09/19	Ascendis Health facility	Mylan	$9,400	CMO
01/03/19	Sterling Pharma Solutions	GHO Capital	Not Disclosed	Full-service API development and GMP manufacturing
01/02/19	Avista Pharma	Cambrex	$252,000	Small-molecule API and finished dose form CDMO

ENDNOTES

Endnote 1

Micklus, "Investment Outlook For Cell And Gene Therapies Is Cautiously Optimistic," – In Vivo, 8 April 2019.

Endnote 2

R. Rader, "Cell and Gene Therapies: Industry Faces Potential Capacity Shortages," Genetic Engineering & Biotechnology News (GEN), 37(20), Nov. 15, 2017.

Endnote 3

Langer, E.S. et al., Report and Survey of Biopharmaceutical Manufacturing Capacity and Production, 15th Edition, BioPlan Associates, April 2018.

Endnote 4

Biosimilars Manufacturing: Key Considerations and Expected Outsourcing Practices (4th Edition), Industry Standard Research.

Endnote 5

Anna Rose Welch, Editor, Biosimilar Development, "Biosimilars, Biobetters, or Both: Report Highlights Manufacturing Considerations," October 19, 2018.

HIGHLIGHTS FROM RECENT RESULTS
COMPILED BY ARGUS RESEARCH

U.S. COMPANIES

BIO TECHNE (TECH)

Quarterly Results Summary

Bio Techne recently reported above-consensus results for fiscal 2Q19. For the quarter, sales grew 13% on a GAAP basis (11% organically) to $175 million, despite a "much tougher" year-earlier comp. The adjusted operating margin narrowed by 250 basis points to 32.5% and was adversely affected by the Exosome acquisition; excluding Exosome, the adjusted operating margin expanded by 260 basis points annually. Adjusted EPS rose 4% to $ 1.06 and topped the consensus forecast of $0.98. In fiscal 2018, sales grew 14% to $643 million, and adjusted EPS rose 22% to $4.54.

The company does not provide earnings guidance.

Segment	% of Sales 2Q19	Segment Growth Rate
Protein Sciences	78%	16%
Diagnostics/Genomics	22%	6%

Business & Customers — 2Q19 Transcript

- Protein Sciences posted 14% organic growth in 2Q19. The Diagnostics & Genomics segment posted organic growth of 2%. The timing of OEM shipments, which negatively impacted sales and margins, should become more favorable for the remainder of FY19.
- Bio Techne posted a second consecutive quarter of 30%-plus growth in China, which lacks comparable domestic life sciences suppliers.
- In Asia, Bio Techne is attaining critical mass for its platforms. Demand for both reagents and instruments continues to grow within these emerging markets, driven by researchers in academia and at biopharma companies.
- In March 2019, National Comprehensive Cancer Network (NCCN) announced the inclusion of Exosome's EPI, a non-invasive, urine-based prostate test, to be used along with PSA and other standard-of-care diagnostics, in testing for prostate cancer.

Capital Strategy and M&A

- Two acquisitions (Quad Technologies and Exosome Diagnostics) were completed in 1Q19. Exosome Diagnostics provides exosome-derived diagnostics to detect numerous cancers and neurological conditions from body fluids, eliminating the need for invasive biopsies.
- Quad Technologies provides biocompatible dissolvable polymer (QuickGel) that captures and activates T-cells.
- In October 2018, Bio-Techne entered into a strategic cooperation agreement with Micropoint Bioscience in Shenzhen, China.

CAMBREX (CBM)

Quarterly Results Summary

Cambrex recently reported results for 4Q18. For the quarter, net sales of $124 million under ASC 606 decreased 29% from $175 million a year earlier, which was unadjusted from the prior ASC 605 standard. Restated for ASC 605, 4Q18 sales would have been $202 million and would have increased 14% year-over-year. Under ASC 606, EBITDA was $33.5 million; excluding the accounting revision and Halo's results and acquisition costs, adjusted EBITDA would have been $70.7 million in 4Q18, compared to $65.1 million a year earlier. Under prior standard ASC 605 for all periods, adjusted EPS of $1.44 rose 14% from $1.26 a year earlier and topped the consensus of $1.37. For all of 2018, net sales of $552 million rose from $534 million, under ASC 605 for all periods; and diluted non-GAAP EPS of $3.07 declined from $3.16 in 2017.

Along with the 4Q18 results, management provided preliminary 2019 guidance under the ASC 606 standard. It now expects 2019 revenue growth of 21%-25%, which under ASC 606 for all periods would imply revenue of $622-$643 million. Management also guided for 2019 adjusted EBITDA of $150-$160 million and non-GAAP net income of $1.87-$2.09 per diluted share.

Business & Customers — 4Q18 Transcript

- The drug substance segment (formerly API, and constituting 89% of revenue) delivered 5% organic and constant-currency top-line growth in 4Q18. Drug substance (formerly finished dosage) revenue of $23 million roughly doubled from $12 million in 4Q17.
- Halo adds finished-dose expertise to Cambrex's active pharmaceutical ingredient (API) leadership, thus strengthening its capabilities as an end-to-end small-molecule CDMO.
- With large pharma companies looking to reduce their small-molecule footprint, Cambrex has a robust and growing small-molecule clinical development pipeline.

Capital Strategy and M&A

- In 3Q18, Cambrex completed the acquisition of Halo Pharma, a leading finished dosage-form CDMO, for $425 million. Halo contributed for slightly more than one full quarter of 2018.
- In January 2019, the company acquired Avista Pharma Solutions from Ampersand Capital Partners for $252 million. Avista expands Cambrex's BPOS business into early-stage small-molecule development and testing services.
- Management believes that combining Halo and Avista with the company's legacy drug substance business positions Cambrex as the leading fully integrated small-molecule CDMO across the entire drug lifecycle.
- Cambrex recently completed expansion of its R&D lab in Milan, Italy, and has a new high-potency API facility in Iowa that is expected to come on line in calendar 2Q19.

CATALENT INC. (CTLT)

Quarterly Results Summary

Catalent recently reported above-consensus results for fiscal 2Q19. For the quarter, sales grew 3% (up 5% in constant currency) to $623 million. Adjusted EBITDA rose 5% from the prior year and the adjusted EBITDA margin rose 40 basis points to 23.4%. Adjusted earnings of $0.45 per share were flat with the prior year but above the consensus of $0.37.

For all of fiscal 2018, revenue of $2.46 billion rose 19% as reported (16% organically) and adjusted EBITDA rose 22% to $454 million.

For fiscal 2019, management reaffirmed its guidance calling for $2.50-$2.59 billion in revenue, implying 2%-5% growth, and $597-$622 million in adjusted EBITDA, implying 32%-37% growth.

Segment	% of Sales 2Q19	Segment Growth Rate
Softgel Technologies	34%	-3%
Biologics & Specialty Drug Delivery	30%	25%
Oral Drug Delivery Solutions	25%	14%
Clinical Supply Services	13%	-25%

Business & Customers — 2Q19 Transcript

- The company's fiscal 2Q19 sales growth was driven primarily by biologics and specialty drug delivery, along with contributions from the Cook Pharmica and Juniper acquisitions.
- Growth continues to be impacted by the adoption of the ASC 606 revenue recognition standard, which impacts sourcing activity within clinical supply services. Excluding this change, 2Q19 revenue would have grown 10% annually in constant currency.
- The Softgel business is performing in line with expectations but continues to be hurt by a worldwide ibuprofen API shortage. Although the supply shortage remains a "challenge," it is improving and should show greater stability by the fiscal fourth quarter.

Capital Strategy and M&A

- In the biologics & specialty drug delivery segment, the integration of the Bloomington site acquired in October 2018 is essentially complete, according to CEO John Chiminski.
- In August 2018, Catalent completed the acquisition of Juniper Pharmaceuticals, a European provider of dose-form development and early-stage manufacturing services.
- Juniper is building on the 2017 Pharmatek acquisition, which has strengthened the company's offerings in formulations, bioavailability solutions, and clinical-scale oral dose manufacturing.

CHARLES RIVER LABS (CRL)

Quarterly Results Summary

Charles River Labs recently reported above-consensus results for 4Q18. For the quarter, sales grew 26% to $602 million; excluding acquisitions and currency effects, organic sales grew 11%. The adjusted operating margin rose to 20.3% in 4Q18 from 19.7% a year earlier. Adjusted EPS rose 6% to $1.49 and topped the consensus forecast of $1.40.

For all of 2018, revenue of $2.27 billion increased 22% from $1.86 billion in 2017. Non-GAAP earnings of $6.03 per diluted share rose 14% from $5.27 in 2017.

Along with the 4Q results, the company provided preliminary guidance for 2019. Charles River expects organic revenue growth of 10.5%-12.0%, and 16%-18% growth assuming the potential acquisition of Citoxlab (see below). Management also guided for adjusted EPS of $6.25-$6.40 on an organic basis and $6.40-$6.55 including Citoxlab.

Segment	% of Sales 4Q18	Segment Growth Rate
Research Models & Services	21%	7%
Discovery & Safety Assessment	60%	42%
Manufacturing Support	19%	10%

Business & Customers — 4Q18 Transcript

- In 4Q18, Charles River reported a second consecutive quarter of double-digit organic revenue growth; double-digit organic growth in 3Q18 was the first since 2008. The company is targeting long-term revenue growth in the high single digits.
- The solid growth in 2H18 reflects a healthy market environment, in which total global biotech funding rose 8% to a record $81 billion.
- Based on organic development and niche acquisitions, the company is well positioned to further develop its role as the premier early-stage CRO with the ability to support clients from the target discovery phase through nonclinical development.
- Demand for Charles River's products and services accelerated during the second half of 2018, positioning the company for further growth in 2019.

Capital Strategy and M&A

- In March 2019, Charles River announced a binding offer to acquire UK-based Citoxlab for approximately $510 million.
- With operations in Europe and North America, Citoxlab is a premier nonclinical CRO, providing early-stage services for biopharmaceutical, medical device, agricultural, and chemical companies worldwide.
- The company's broad portfolio has been enhanced by the acquisitions of MPI Research, KWS BioTest, and Brains On-Line.

ICON PLC (ICLR)

Quarterly Results Summary

Icon recently reported below-consensus results for 4Q18. For the quarter, and excluding the adoption of ASC 606, sales grew 7% to $680 million. The adjusted operating margin (excluding ASC 606) of 21.1% rose 140 basis points from the prior year. Fourth-quarter EPS increased 13% to $1.62, two cents above the consensus forecast. Based on the "net business wins" ratio, book-to-bill was 1.25 in 4Q18 and 1.27 for all of 2018. The 2018 closing backlog was a record $5.4 billion, up 10% year-over-year.

For all of 2018, revenue of $2.60 billion was up 8% from 2017, with all periods measured under the prior ASC 605 standard. Full-year earnings before nonrecurring charges increased 14% to $6.16 per diluted share.

Icon reaffirmed its 2019 guidance first issued in January. With all comparisons under the new ASC 606 revenue recognition standard, the company expects revenue of $2.735-$2.835 billion, which at the $2.785 billion midpoint would be up 7% year-over-year. It projects non-GAAP EPS of $6.69-$6.89, which would be up 9.9%-13.1% from 2018.

Business & Customers — 4Q18 Transcript

- Net business awards of $607 million in 4Q18 were an all-time record for the company.
- Management expects overall pharma R&D spending to grow 3% annually. It expects CRO industry revenue to increase at a faster 6% annual rate, as pharma companies outsource additional services.
- The OneSearch platform helps Icon analyze key performance data to identify optimal trial sites. Icon's medium-term goal is to more than double the recruitment rate while halving start-up times at new sites.

Capital Strategy and M&A

- In January 2019, Icon signed an agreement to acquire MolecularMD. The acquisition expands Icon's capabilities into molecular diagnostic testing, immunohistochemistry, and companion diagnostics for precision medical research.
- Icon also extended its master services agreement with Pfizer, designed to help Pfizer advance its development pipeline rapidly and efficiently.
- Icon's ability to manage projects under various flexible outsourcing models is leading to new business opportunities.
- In 2018, Icon repurchased $129 million of its stock.

ILLUMINA INC (ILMN)

Quarterly Results Summary

Illumina recently reported below-consensus EPS for 4Q18. Fourth-quarter revenue rose 12% from the prior year to $867 million. The non-GAAP operating margin declined 710 basis points to 24.3%. Adjusted EPS of $1.32 declined from $1.44 a year earlier and missed the consensus forecast by $0.04.

For all of 2018, revenue of $3.33 billion rose 21% from $2.75 billion in 2017, and adjusted diluted EPS of $5.72 rose 43%.

Along with the 4Q18 results, management provided 2019 guidance. Management expects 13%-14% revenue growth, which implies sales of $3.77-$3.80 billion. Illumina also projects non-GAAP EPS of $6.50-$6.60, which implies growth of 13.6%-15.4%.

Segment	% of Sales 4Q18	Segment Growth Rate
Product	85%	12%
Service & Other	15%	8%

Business & Customers — 4Q18 Transcript

- Illumina generated 8% growth in sequencing consumables, with annual growth in the high-, mid- and low-throughput categories. After normalizing for stocking orders, year-over-year growth was 16%.
- Both sequencing and microarray instrument revenue grew in the double digits. Illumina should benefit from the 2018 decision by the Centers for Medicare & Medicaid Services to provide Medicare coverage for NGS testing of certain cancer patients.
- Although 225 petabytes of sequencing data have been generated on Illumina platforms, less than 1% of the human genome has been mapped, signaling a vast opportunity for genetic sequencing equipment and services.

Capital Strategy and M&A

- In November 2018, Illumina agreed to acquire Pacific Biosciences, a device company focused on long-read sequencing technologies. Illumina is strong in short-read platforms, so the Pacific Biosciences acquisition will be synergistic and complementary.
- Illumina is currently managing product transitions, from HiSeq (high-end) sequencers to MiniSeq and NextSeq (less-expensive, desktop machines), while also shifting high-end users to NovaSeq, its most advanced option.

IQVIA (IQV)

Quarterly Results Summary

IQVIA recently reported above-consensus results for 4Q18. Fourth-quarter revenue of $2.67 billion rose 7% on a reported basis and 8% in constant currency. Adjusted EBITDA rose 11%, and the adjusted EBITDA margin expanded by 80 basis points to 21.7%. Adjusted EPS rose 23% to $1.50 and beat the consensus by $0.03.

For all of 2018, revenue of $10.4 billion increased 7% on a GAAP basis and in constant currency. Adjusted EBITDA of $2.22 billion increased 11% on a GAAP basis and 10% in constant currency. Non-GAAP diluted EPS of $5.55 increased 22%.

Along with its 4Q18 results, management provided guidance for 2019. With comparisons for all periods under accounting standard ASC 606, the company expects revenue growth of 5.8%-7.9% in constant currency and 4.7%-6.8% on a GAAP basis, implying 2019 revenue of $10.90-$11.12 billion. IQVIA also guided for non-GAAP EPS of $6.20-$6.40, implying growth of 11.7%-15.3%.

Segment	% of Sales 4Q18	Segment Growth Rate
Technology & Analytics	42%	9%
R&D Solutions	51%	8%
Contract Sales & Medical	7%	-7%

Business & Customers — 4Q18 Transcript

- IQVIA continues to sign new clients to its Orchestrated Customer Engagement (OCE) platform. In mid-October 2018, it signed Roche Pharma to a multiyear OCE contract spanning more than 100 countries and 14,000 users; other major wins in 2018 included Novo Nordisk.
- Since its launch in December 2017 with partner Salesforce.com, the OCE platform has registered over 30 competitive wins and now has more than 30,000 users in 100-plus countries.
- IQVIA is also working with Salesforce.com on Orchestrated Clinical Trials (OCT), which will provide regulated content management, regulatory compliance, and virtual clinical trials.

Capital Strategy and M&A

- In 4Q18, IQVIA passed the anniversaries of several businesses that were acquired in 2017, leading to slower nonorganic revenue growth.
- IQVIA has signed a collaboration agreement with Genomics England, which will assemble the world's largest pool of linked clinical whole-genome sequence data available for research.
- The IQVIA Technology & Analytics unit is benefiting from significant contract wins with top-five pharma companies.

LABORATORY CORP OF AMERICAN HOLDINGS (LH)

Quarterly Results Summary

Laboratory Corp. of America Holdings (LabCorp) recently reported above-consensus non-GAAP EPS for 4Q18. Fourth-quarter revenue of $2.8 billion rose 2% from the prior year. Adjusted operating income of $395 million fell 9%, and the adjusted operating margin narrowed by 150 basis points to 14.2%. Adjusted EPS of $2.52 rose 11% from the prior year and topped the consensus forecast by $0.03.

For all of 2018, revenue of $11.33 billion increased 10%, with 7% from M&A and 3% from organic growth and currency translation. The adjusted operating margin of 15.2% narrowed from 16.2% a year earlier. Adjusted earnings of $11.02 per diluted share rose 20% from 2017.

Management provided guidance for 2019, with all comparisons under accounting standard ASC 606. LabCorp. expects revenue growth of 0.5%-2.5% and non-GAAP EPS growth of 0%-3%, to $11.00-$11.40. It projects free cash flow of $950 million to $1.05 billion, compared to $926 million in 2018.

Segment	% of Sales 4Q18	Segment Growth Rate
LabCorp Diagnostics	61%	-3%
Covance Drug Development	38%	9%

Business & Customers — 4Q18 Transcript

- LabCorp's 4Q18 performance was driven by Covance, which generated a 1.34 book-to-bill ratio and 290 basis points of margin expansion. Book-to-bill under the prior ASC 605 revenue recognition standard would have been 1.46 for Covance.
- Covance, according to LabCorp, is the only contract research organization to combine early development, central lab and clinical services in an end-to-end offering.
- The Diagnostics business in 4Q18 was burdened by nonoperational items that collectively led to a 400-basis-point decline in the segment operating margin, according to CEO David King.

Capital Strategy and M&A

- In February 2019, LabCorp announced details on Phase II of its LaunchPad initiative in Diagnostics, designed to digitize the business and reduce costs.
- The LabCorp-Walgreens partnership plans to open 125 locations by the end of 2019 and to have 600 locations in operation within four years.
- In 4Q18, the company completed the divestiture of Food Solutions at an attractive valuation.
- In 2019, LabCorp expects to deploy additional capital for share buybacks.

MEDPACE HOLDINGS INC. (MEDP)

Quarterly Results Summary

Medpace Holdings (Medpace) recently reported above-consensus results for 4Q18. Fourth-quarter revenue of $192 million under ASC 606 rose 82% from the prior year; under the prior standard of ASC 605, revenue of $146 million increased 29%. Adjusted EBITDA under ASC 605 increased 43% to $38.6 million, while the EBITDA margin expanded by 300 basis points to 30.2%. Adjusted EPS totaled $0.75 under ASC 605, rising 92% from the prior year. Adjusted earnings beat the consensus estimate by $0.08.

For all of 2018, and under the prior accounting standard ASC 605 in order to maintain comparability, Medpace posted net service revenue of $478 million, reflecting growth of 24% from $387 million in 2017. Non-GAAP EPS rose 85% to $2.81.

Along with its 4Q results, Medpace provided 2019 guidance with all comparisons under ASC 606. Management forecast revenue of $783-$807 million, representing growth of 11.1%-14.5% from 2018 under ASC 606. The company expects 2019 adjusted earnings of $2.58-$2.69 per diluted share.

Business & Customers — 4Q18 Transcript

- According to CEO August Troendle, Medpace saw a significant softening in its overall business environment in the fourth quarter of 2018. The cancellation rate in 4Q18 was roughly twice the rate seen in the first three quarters of 2019.
- The environment shows signs of stabilizing in 1Q19, according to the CEO. Revenue should increase on a year-over-year basis going forward, though growth is expected to slow from 2018.
- Rapid revenue growth prevented margin contraction in 2018. However, margin contraction is expected beginning in 1Q19, and the CEO said Street margin assumptions for the full year were too high.

Capital Strategy and M&A

- Medpace continues to expand its global infrastructure while engaging in business development activities. The company remains focused on serving small and mid-sized biopharma customers.
- Medpace continues to benefit from low customer concentration. Top 5 customers represented just 22% of 2018 revenue, while top 10 customers were just 33%.

PRA HEALTH SCIENCES INC. (PRAH)

Quarterly Results Summary

PRA Health Sciences recently reported above-consensus non-GAAP EPS for 4Q18. Fourth-quarter revenue of $730 million under ASC 606 rose 11% (12% in constant currency). Adjusted EBITDA grew 18% to $136.2 million, while the adjusted EBITDA margin (under ASC 606) expanded to 18.7% from 17.5% a year earlier. Adjusted net income of $1.31 per share rose 26% year-over-year and beat the consensus by $0.04.

For all of 2018, PRA Health Sciences reported revenue of $2.87 billion, up 27% from 2017; on a comparable basis under ASC 605 for all periods, revenue would have been $2.61 billion for 2018 and would have risen 18% (17% in constant currency). Adjusted net income of $4.28 per diluted share rose 29% from 2017.

Along with the 4Q18 results, management provided guidance for 2019; all guidance and comparisons are under ASC 606. The company expects revenue of $3.09-$3.20 billion, which assumes as-reported and constant-currency growth of 8%-11%. Management also projects full-year non-GAAP earnings of $4.93-$5.08 per diluted share, representing growth of 15%-19%.

Business & Customers — 4Q18 Transcript

- Net new business wins for 4Q18 rose 3% year-over-year. Strong order trends led to a net book-to-bill ratio of 1.3, extending the company's multiquarter run of book-to-bill ratios exceeding 1.2.
- The backlog rose 4% sequentially and 20% from the prior year, finishing 2018 at approximately $4.2 billion. The backlog does not include the Data Solutions segment.
- New business awards show healthy diversity, with 58% from the pharmaceutical sector and 42% from biotech.

Capital Strategy and M&A

- In 2016, PRA began its relationship with Japan's Takeda, which is selling its Chinese JV prior to its $62 billion purchase of Ireland's Shire plc. PRA does not anticipate any impact on studies it is currently running for Takeda and looks forward to continuing its Takeda partnership for a fourth year.
- The integration of Symphony Health, acquired in September 2017, is progressing as planned.
- In 2Q18, PRA amended its A/R financing agreement, which increased borrowing capacity and extended the maturity date.

SYNEOS HEALTH INC. (SYNH)

Quarterly Results Summary

Syneos Health recently reported above-consensus non-GAAP EPS for 4Q18. Fourth-quarter revenue under ASC 606 was $1.15 billion; under ASC 605, revenue of $834 million rose 11%. The adjusted EBITDA margin under ASC 605 increased 230 basis points to 22.3%, and adjusted EBITDA under ASC 605 rose 19% to $186 million. Adjusted EPS under ASC 606 rose 35% year-over-year to $0.95, and came in $0.14 above the consensus forecast. For comparability purposes, adjusted 4Q18 EPS under ASC 605 was $1.05.

For all of 2018, Syneos Health reported revenue of $4.39 billion under ASC 606; reported revenue rose 137% from the prior year. As measured under ASC 605 for all periods, 2018 revenue would have been $3.18 billion and would have been up 3% from $3.10 billion in 2017 (which includes a pro forma contribution from InVentiv Health, acquired in August 2017). Adjusted net income of $2.87 per diluted share rose 26% year-over-year.

Along with the 4Q18 results, management provided guidance for 2019; all guidance and comparisons are under ASC 606. Syneos Health forecast revenue of $4.62-$4.73 billion, representing growth of 5%-8%%. Management also projects full-year adjusted EBITDA of $625-$660 million; and non-GAAP earnings of $3.03-$3.23 per diluted share, representing growth of 6%-13% from 2018.

Segment	% of Sales 4Q18	Segment Growth Rate
Combined Clinical Solutions	73%	3%
Combined Commercial Solutions	27%	18%

Business & Customers — 4Q18 Transcript

- Syneos is seeing strong customer engagement based on the breadth of its biopharmaceutical outsourcing offerings.
- Commercial Solutions posted 18% annual revenue growth in 4Q18, while Clinical solutions boosted its year-ending backlog by 14%.
- Syneos posted total net new business awards of $3.90 billion under ASC 605 for all of 2018.
- The book-to-bill ratio was 1.22 for the full year, including a 1.25 clinical book-to-bill and a 1.16 commercial book-to-bill.

Capital Strategy and M&A

- Syneos, which was formed in August 2017 from the combination of InVentiv and INC Research, has achieved $76 million in annual integration synergies to date and is on track to achieve $125 million in synergies annually by 2020, according to CEO Alistair MacDonald.
- The company continues to invest in its Syneos One offering (formerly Integrated Solutions), which collaborates across business units to create custom solutions.
- In 3Q18, Syneos completed its acquisition of Kinapse, which expands its regulatory, safety, and pharmacovigilance consulting services in the post-approval space.

THERMO FISHER SCIENTIFIC (TMO)

Quarterly Results Summary

Thermo Fisher recently reported above-consensus non-GAAP earnings for 4Q18. Fourth-quarter revenue of $6.5 billion grew 8% on a GAAP basis and 8% organically, as M&A and currency offset one another. Adjusted operating income grew 12% from the prior year; the adjusted operating margin narrowed by 10 basis points to 23.1%. Adjusted EPS increased 16% to $3.25 and topped the consensus forecast by $0.07.

For all of 2018, revenue of $24.4 billion increased 16% on a reported basis and 8% on an organic basis. Non-GAAP EPS totaled $11.12, up 17% from 2017.

Management also issued sales and EPS guidance for 2019. The company forecast revenue of $24.88-$25.28 billion, which implies 2%-4% growth. Thermo forecast 2019 non-GAAP diluted EPS of $12.00-$12.20, which implies 8%-10% growth.

Segment	% of Sales 4Q18	Segment Growth Rate
Life Sciences	26%	8%
Analytical Instruments	24%	11%
Specialty Diagnostics	15%	4%
Laboratory Products	40%	8%

Business & Customers — 4Q18 Transcript

- Management noted that sales to pharmaceutical and biotech customers grew at a low-teens rate in 4Q18, while revenue from academic and government customers rose in the mid-single digits for the quarter and year.
- The three pillars of Thermo Fisher's growth strategy are high-impact innovation, built around new product launches; a focus on high-growth emerging markets, led by China; and efforts to enhance the customer value proposition.
- In 2Q18, the company opened a Precision Medicine Science Center to help U.S. customers strengthen their capabilities in genomic, proteomic and metabolomic analysis.

Capital Strategy and M&A

- In March 2019, Thermo Fisher agreed to acquire Brammer Bio from private equity firm Ampersand Capital Partners for $1.7 billion.
- Brammer is expected to generate $250 million in 2019 revenue while exceeding the projected market growth rate of 25% for the medium term.
- In January 2019, Thermo announced the sale of its Anatomical Pathology business. While that sale is included in the 2019 guidance, the Brammer Bio acquisition is not.
- In October 2018, Thermo Fisher completed the purchase of Becton Dickinson's Advanced Bioprocessing business for $477 million in cash. The acquisition adds complementary cell-culture media products, along with $100 million in annualized revenue.

FOREIGN COMPANIES

DOTTIKON ES HOLDINGS AG (DESN)

Semiannual Results Summary

Switzerland-based Dottikon reports semiannually in Swiss Francs (CHF). Dottikon reported lower 1H18 revenue and net income. Net sales of CHF 56.6 million were down 19% from the prior year. Production output (net sales plus inventory changes in semi-finished and finished goods) declined 11%. EBITDA of CHF 9.8 million fell 51% year-over-year. First-half IFRS net income of CHF 2.0 million declined substantially from CHF 9.6 million a year earlier.

Along with the 1H18 results, management provided guidance for the full year. Due to delayed net sales realizations in the first half, and despite a projected business recovery in the second half, the company now expects lower net sales and net income in FY18.

Business & Customers – 1H18

- Management attributed the company's disappointing first-half performance to geopolitical and economic uncertainties, the intermittent scale-up of business processes, and supply bottlenecks due to the enforcement of environmental regulations.
- Several Asian chemical producers were hurt by the temporary or permanent closure of facilities due to environmental issues, leading to disruptions in sourcing.

Capital Strategy and M&A

- Dottikon reaffirmed its focus on serving customers as a strategic development and manufacturing partner and its specialist role for hazardous reactions.

EUROFINS SCIENTIFIC (ERF)

Annual Results Summary

Luxembourg-based Eurofins Scientific reports semiannually in euros. Eurofins reported 2018 revenue of 3.78 billion euros, up 27% from 2017 despite a 3% currency headwind. Revenue rose 4.5% on an organic basis. Core (non-IFRS) EBITDA of 720 million euros grew 29% year-over-year and represented 19.0% of 2018 revenue versus 18.7% in 2017. Core net income of 20.11 euros per diluted share rose 15% from the prior year.

At 2018 average exchange rates, Eurofins management announced the following full-year 2019 objectives. The company forecast revenue of 4.5 billion euros, implying 18% growth (5% organic) from 2018. That forecast was raised from prior midyear guidance of 4.39 billion euros. Management guided for core EBITDA of 850 million euros, which would be up 18% year-over-year and imply a core EBITDA margin of 18.9%.

The company continues to target a core EBITDA margin of 20% by 2020, as reflected in preliminary guidance of 5.0 billion euros in revenue and 1.0 billion euros in adjusted EBITDA for 2020.

Business & Customers — 2H18

- Eurofins' services across four platforms (food, environment, clinical, and pharmaceutical) have high barriers to entry. The company's bioanalytical business is highly scalable and benefits from a global network of laboratories.
- The company is more than halfway through its current five-year growth plan, with the goal of building a one-of-a-kind laboratory infrastructure platform.
- Eurofins doubled revenue multiple times between 2005 and 2018 and grew EBITDA more than twelvefold during this period.
- In 2019 and 2020, according to CEO Gilles Martin, Eurofins will de-emphasize M&A as most strategic acquisitions have been completed, and will instead focus on operational excellence. We thus expect top-line growth to slow while profitability improves.

Capital Strategy and M&A

- In December 2018, Eurofins closed the $175 million acquisition of TestAmerica, which it called the leading environmental testing laboratory group in North America.
- In August 2018, Eurofins completed the $670 million acquisition of Covance Food Solutions from LabCorp (NYSE: LH). The acquisition brings a network of 12 Covance Food Solutions test & safety facilities across the globe.

EVOTECH AG (EVT)

Annual Results Summary

Germany-based Evotech reports semiannually in euros; the company has discontinued its quarterly update. Evotech reported 2018 revenue of 375 million euros, up 42% from the prior year. Core (non-IFRS) EBITDA grew 67% and represented 25.4% of revenue, up from 21.7% in 2017. IFRS net income of 0.56 euros per diluted share rose strongly from 0.16 euros a year earlier.

Along with the 2018 results, management provided guidance for 2019. Group revenues are expected to increase approximately 10% year-over-year. Adjusted EBITDA is also forecast to grow approximately 10%.

Business & Customers – 2018

- Evotech acquired Aptuit in August 2017 and Evotech ID (Lyon) from Sanofi in July 2018.
- The company has strengthened its partnership with Celgene in oncology, and in September 2018 expanded this partnership to include targeted protein degradation.

LONZA GROUP (LONN)

Semiannual Results Summary

Switzerland-based Lonza Group reports semiannually in Swiss Francs (CHF). Lonza reported 2018 revenue of CHF 5.54 billion, which was up 9% from 2017. All comparisons now include Capsugel. Core (non-IFRS) EBITDA of CHF 1.51 billion grew 12% from 2017. Core net income of CHF 11.93 per diluted share rose 11% year-over-year.

Along with the 2018 results, management provided directional rather than explicit full-year 2019 guidance along with a three-year outlook to 2022. The company expects mid- to high single-digit revenue growth in 2019, along with sustained high core EBITDA margins. Its guidance for 2022, still including the water care business, calls for annual sales of CHF 7.5 billion, a core EBITDA margin of 30%, and double-digit returns on invested capital.

Segment	% of Sales	2018 Segment Growth Rate
Pharma&Biotech	56%	29%
Specialty Ingredients	44%	14%

Business Outlook

- On a segment basis, objectives include high single-digit sales growth for Pharma & Biotech with a 30%-plus core EBITDA margin; mid- to high single-digit sales growth for Specialty Ingredients/Consumer Health, with margins rising from the high 20s to more than 30%; and low to mid-single-digit sales growth for Specialty Ingredients/Consumer & Resources Protection, with margin progression from the high teens to more than 25%.

Capital Strategy and M&A

- In November 2018, Lonza announced plans to divest its water care business to private equity firm Platinum Equity for $630 million. Inclusion of the French water care business in this deal is still under discussion.
- The divestiture of water care strengthens Lonza's focus on its healthcare continuum strategy.

SIEGFRIED HOLDINGS AG (SFZN)

Semiannual Results Summary

Switzerland-based Siegfried Holdings AG reports semiannually in Swiss Francs (CHF). Siegfried Holdings reported 2018 revenue of CHF 794 million, which was up 6% (4% in local currency) from CHF 751 million in 2017. EBITDA of CHF 127 million rose 15% annually, and the EBITDA margin widened by 120 basis points to 16.0%. IFRS net income of CHF 13.38 per diluted share rose 34% from 2017.

Along with its 2018 results, management provided full-year guidance for 2019. It expects to grow revenue at least in the mid-single-digit range and to continue to expand EBITDA margins.

Segment	% of Sales	2018 Segment Growth Rate
Drug Substances	75%	2%
Drug Products	25%	17%

HIGHLIGHTS FROM RECENT RESULTS (CONTINUED)
COMPILED BY ARGUS RESEARCH

BPOS VALUATION TABLE

		Fundamentals				Growth Rates				Valuations			
	Ticker	Mkt. Cap ($BIL)	Revenue ($BIL)	Op Mgn (%)	D/E (%)	Rev %	EPS %	1-Yr Return (%)	5-Yr Return (%)	PS	PE	EV/ EBITDA	Yield (%)
US COMPANIES													
Bio-Techne Corp.	TECH	7.3	0.7	22.3	50	13	11	30	129	10.7	38.0	38.4	0.7
Cambrex Corp.	CBM	1.3	0.6	20.9	46	17	15	-27	112	2.5	20.3	10.1	0.0
Catalent Inc.	CTLT	5.8	2.5	12.4	141	3	6	-1	102	2.4	19.6	15.2	0.0
Charles River Laboratories International, Inc.	CRL	6.8	2.6	15.9	125	14	7	30	127	3.0	19.4	16.2	0.0
ICON Public Limited Company	ICLR	7.2	2.8	14.9	26	8	12	9	189	2.8	17.5	15.3	0.0
Illumina Inc.	ILMN	44.4	3.8	26.5	51	14	14	24	112	13.3	40.3	40.8	0.0
Iqvia Holdings Inc.	IQV	27.6	11.0	8.0	158	6	14	38	181	2.7	19.3	21.3	0.0
Laboratory Corporation of America Holdings	LH	14.8	11.2	12.8	87	1	2	-9	53	1.3	12.6	10.9	0.0
Medpace Holdings Inc.	MEDP	2.0	0.8	14.3	18	13	12	57	103	2.9	19.3	15.2	0.0
PRA Health Sciences Inc.	PRAH	6.9	3.1	11.0	103	9	17	24	420	2.4	18.3	18.7	0.0
Syneos Health Inc.	SYNH	5.2	4.7	6.3	99	6	9	34	127	1.2	13.9	14.4	0.0
Thermo Fisher Scientific Inc.	TMO	107.0	25.2	16.0	69	3	9	28	126	4.4	19.9	20.2	0.3
Averages		*19.7*	*5.7*	*15.1*	*81.1*	*9*	*11*	*20*	*148*	*4.1*	*21.5*	*19.7*	*0.1*
FOREIGN COMPANIES													
Dottikon ES Holding AG	DESN	0.5	0.1	17.3		-19	-51	-34	117	4.8	40.0		NA
Eurofins Scientific	ERF	6.4	4.4	11.4	116	17	15	-20	66	1.7	37.8	12.9	0.7
Evotech AG	EVT	3.3	0.4	22.0	38	11	125	39	479	9.1	52.3	35.6	NA
Lonza Group Ltd.	LONN	22.1	5.5	27.3		9	11	21	254	4.0	24.5		NA
Siegfried Holding AG	SFZN	1.5	0.8	16.0	16	6	34	11	114	1.9	26.9	12.4	0.7

Sources: Argus Research, Bloomberg Inc. Data as of 3/29/2019

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