2023 the year of re-alignment: yet all data points to green shoots ahead for 2024

An indpeth analysis on the health of the CRO/CDMO sector

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Introduction

In last year's CPHI Annual Report, the health of the CRO/CDMO sector was covered, and the question asked, "Has the bubble burst?" on the explosive growth observed in the years leading up to, and including, the pandemic. The prediction was for continued, but modulated, strength in demand for Pharma Services in the near and mid-term. Given that biotech funding levels appeared to be "bottoming out" at pre-pandemic (historically robust) levels, emerging pharma still sitting on 2-3 years of cash reserves, and the amount of cash sitting in big pharma's war chest, demand would remain relatively strong, albeit somewhat muted versus the past two years. As long as global pandemics and geopolitical tensions were in check, the sector appeared to be weathering the storm.

This year, we will look at the past 12 months, and update our predictions on both the near and long term health of the sector. Generally speaking, with the pandemic mostly behind us, global geopolitical tensions appearing in check, the level of demand has generally not lived up to expectations. With some exceptions, CRO's and CDMO's are seeing a softening in demand (particularly from emerging pharma and in earlier phases of development) which we believe will extend well into 2024. In spite of the current softness, the underlying demand drivers remain very strong for the sector. As such, the years 2023 and 2024 are viewed as a period of re-calibration or re-alignment. So what has happened since CPHI last year? Let's take a look.

Demand for Pharma Services and the Long-term Outlook

Before we look at the current demand for CRO/CDMO services, it is important to understand the long-term growth drivers for the industry. Over the past 10 years, the number of molecules in the R&D pipelines has more than doubled (Figure 1), with growth rates for small and large molecules around 5% and 12% CAGR respectively. The split between small and large molecules in development pipelines is approaching 50-50. Generally speaking, with the average drug taking over 10 years to go from

discovery to commercialization, the molecules in the development pipelines of today represent a key demand driver for the CRO/CDMO industry for the next decade, and both small molecule and large molecule services will be required to progress these new therapeutics.

Number of Molecules in R&D Pipelines Globally

Figure 1: Piper Sandler & Co.; IQVIA

One of the major contributors to growth in the CRO/CDMO sector is the emerging pharma / biotech community. By definition, these companies need to outsource most, if not all, of their R&D and manufacturing requirements to service providers, many of whom are attending CPHI Worldwide this year. Figure 2 demonstrates the importance of emerging pharma to the current and future success of the global pharma industry's innovative new therapeutic development.

Emerging Biopharma's (EPB's) Contribution to Pharma Pipelines

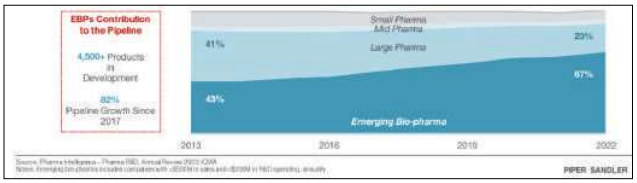

Figure 2: Piper Sandler & Co, IQVIA

What's Going on with Emerging Pharma?

A proxy for the health of the demand for CRO/CDMO sector is funding levels into the biotech / emerging pharma sector. After a period of significant decline (vs 2020/21), funding into the sector seems to have stabilized over the past two quarters at levels seen just prior to the pandemic (Figure 3). Q2 2023 saw funding into the sector of $12.0 billion which was down only 3% y/y. Many in the industry have been asking when/where the funding "trough" would bottom out. If, in fact, we've reached the bottom, then one level of uncertainty (risk) will be reduced, and more predictability can be factored into the future spending habits of emerging pharma. Will a belt loosening ensue?

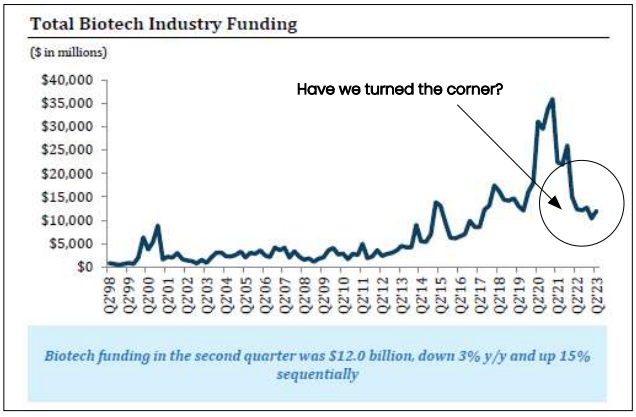

Figure 3: William Blair Equity Research. July 2023

Taking a closer look at funding into the sector (Figure 4) shows a mixed bag with VC, Follow-ons, and PIPE's all resuming near normal growth trends, albeit starting from pre-pandemic levels (2019). However, IPO's remain anemic through the first half of 2023 down 6% y/y. Total funding into the sector through July is $30.2 Bn and full year 2023 is trending ahead of 2022.

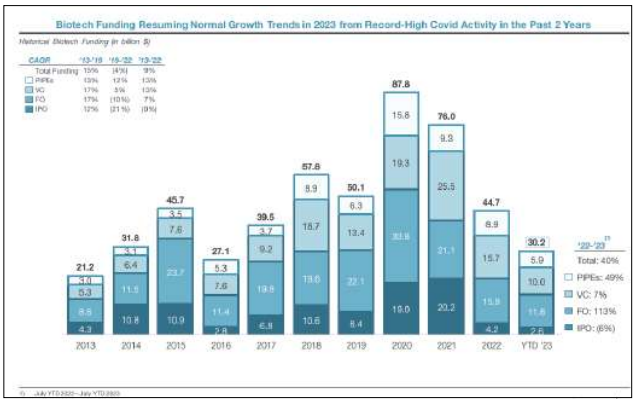

Figure 4: Piper Sandler & Co. September 2023

Too Many Companies, Too Little Capital:

Although non-IPO funding appears to have stabilized, there are still too many emerging pharma companies vying for too little capital. The number of companies with active R&D pipelines globally has grown from nearly 4800 in 2020 to over 5500 in 2023 (Figure 5). That's an increase of nearly 15%, while funding levels have dropped to nearly half the 2020 levels during the same period.

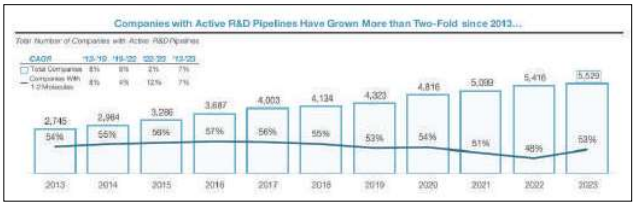

Figure 5: Piper Sandler & Co. September 2023

As a result of this, two things have happened:

1. Emerging pharma companies are reassessing their R&D product pipelines and will need to evaluate their approach in order to continue, or pause, slower growth programs to maintain a financial cushion to ensure that their lead compounds take the lions share of the resources. This equates focusing cash burn on fewer programs – reducing CRO/CDMO demand.

2. Emerging pharma valuations have become subdued. Since the second half of 2022 and extending through the first half of 2023, the prevalence of down rounds has accelerated dramatically (Figure 6) with at least one-third of venture growth-stage companies and over 10% of late stage companies in down rounds.

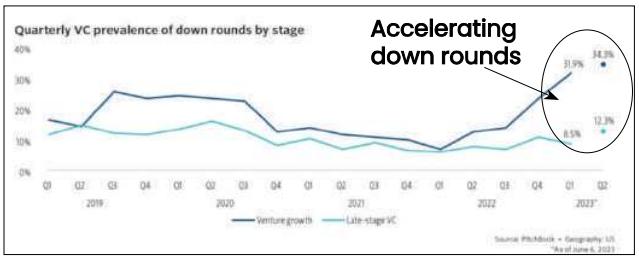

Figure 6: Pitchbook. June 2023.

The capital supply and demand dynamic is out of balance. According to Pitchbook, the demand for capital at late-stage biotechs is nearly 3x the supply, and demand for capital at venture growth-stage companies is 1.3x supply.

IPO Exits are Clogged:

Contributing to the challenge is the IPO market is clogged (Figure 7). Investors who saw a pathway to exit just two years ago are now stuck until the valuations come back. There is some evidence that IPO's are starting to pick up, but it will take time until the structural imbalances work their way through and get back to a more robust opportunity for IPO exits. For now, the system is clogged.

Figure 7: Pitchbook NVCA Monitor. March 2023.

To cure this, any combination of three factors has to happen: 1) VC/non-public funding needs to increase; 2) IPO's need to increase; 3) the number of biotechs need to decrease (fold, M&A, reverse merge). The result for now is an investor's market.

How Long is the Cash Runway for Biotechs?

Given the biotech funding environment mentioned above, CRO's and CDMO's are left wondering how much cash runway is remaining within the emerging pharma sector should the anemic funding environment continue on a protracted basis. Last year, we reported that emerging pharma was sitting on about 2-3 years of cash. According to KPMG and CapIQ (Figure 8), the US emerging pharma cash runway is just under two years (20 months), down from over 36 months in Q1 2021.

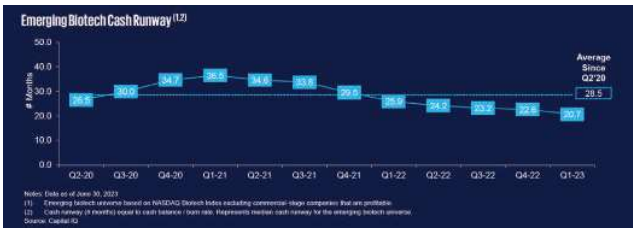

Figure 8: KPMG Corporate Finance and CapIQ. US Biopharma Services Industry Update H1 2023

Implications for CRO/CDMO's:

The protracted, weaker VC funding environment, and a clogged IPO exit funnel has led emerging pharma companies to continue to focus on managing cash burn. According to Pitchbook's European Venture Report for H1, 2023, they have seen VCs work with their portfolios to restructure operations in-house and extend cash runways as far down the line as they can given current funding environment. This has translated into a continued softening in demand for pharma services, particularly in the early and mid phases of development where most emerging pharma companies engage with the pharma services sector. With some exceptions, the general consensus among most of the CRO/CDMO's we've spoken to is a broad softening of the market, with most citing a softening in demand from emerging pharma.

What's Going On at Big Pharma?

While much attention has been paid to VC funding and emerging pharma, big pharma has been going through its own reinvention. Big pharma is operating against backdrop of continuing inflationary pressures, rising capital costs, patent expiries, ongoing Federal Trade Commission (FTC) transaction scrutiny, and the impact of the Inflation Reduction Act (IRA) in the US. In a recent survey by PwC, 90% of executives said they were worried about the macroeconomic environment, with many already taking action to adjust strategic plans.

M&A Picking up:

In last year's CPHI report, I predicted M&A to likely increase significantly as big pharma's balance sheets were robust, patent cliff's coming, and value buying opportunities with emerging pharma accelerating. What's happened thus far in 2023?

According to Goldman Sach (Report July 6, 2023), pharmaceutical companies are sitting on $700 billion for acquisitions and investment. Larger strategic consolidations have picked up in the past year, with a number of notable deals including Pfizer-GBT, Amgen-Horizon, GSK-Bellus, Merck-Prometheus, and Pfizer-Seagen. It is likely that these larger consolidations will continue for the foreseeable future. As big pharma continues to shore up gaps in therapeutic areas, and as it looks for new technology areas emerging earlier in the discovery pipelines.

Big pharma's M&A of smaller emerging pharma companies (values <$1Bn) has been more muted than expected for the past year, although there are signs of acceleration over the first two quarters of 2023. With IPO exits clogged, M&A activity should continue to increase, and value-buying opportunities of pre-IPO emerging biopharma should accelerate given the capital supply/demand dynamic currently ongoing in the private funding market.

Streamlining for the Future:

As big pharma deals with increasing costs, recent government intervention around mega M&A deals and drug pricing controls, and a changing macro environment, it is beginning a phase of structural change to ***proactively*** get in front of the changing dynamic. One area gaining much attention this year is announced layoffs within the industry. According to a Fierce Biotech analysis, as of mid-August 2023, layoffs industrywide (119) have eclipsed all of 2022. While understandable for emerging pharma, several big pharma companies including Novartis, Biogen, BMS, J&J, Genentech, Takeda, Novo, Eisai, Merck KGaA have all announced planned layoffs in 2023. A notable example is Biogen's "Fit for Growth" program where President & CEO Christopher A. Viehbacher mentioned, "We have taken a bottom-up view to shift our resources to the areas of greatest value creation." In August, Biogen announced ~11% reduction in workforce (~1000 employees) over the next three years.

Implications for CRO/CDMO's:
Big Pharma Streamlining - Enhances Demand for Services: As big pharma streamlines its resources to areas of greatest value creation (shedding people and assets) the need for outsourced providers of research, development, and manufacturing services will be needed more than ever. We should bolster demand for CRO/CDMO's.

Big Pharma M&A - Enhances Demand for Services: Increasing M&A volume provides an outlet for the clogged IPO funnel currently observed in the emerging pharma sector. This keeps the flow of capital to support development programs and commercialization of new therapeutics innovated by emerging pharma, and bolsters demand for CRO/CDMO's. This also helps fix the capital supply/demand imbalance in the emerging pharma sector by reducing the number of companies. Currently there are too many companies are chasing too little cash.

Government Regulatory Environment and The Inflation Reduction Act:

While government price controls have been the norm in many countries around the globe, the pharma industry in the US has relied on the ability to fuel the heavy cost of innovative drug development (now >$2Bn per new drug launched) by playing in an environment of limited price controls. This has enabled an environment of hyper-fueled re-investment of pharma profits back into R&D or M&A, and many argue has been the catalyst for the explosive decades of innovation centered in US.

The Inflation Reduction Act

In August of 2022, the Inflation Reduction Act (IRA) was passed in the US. Among other things, the IRA requires the US government to negotiate prices for the top-spending Medicare drugs. In August 2023, the first 10 drugs up for price negotiation were announced, and notably, number of drugs eligible for government price negotiations will increase to 60 drugs by 2029. The law sets the drug price ceiling at between 25% and 60% of its list price, with no price floor.

Another element of the IRA is the timing of when a drug will be eligible for government price negotiation. Under the IRA small molecules can be selected for government price negotiations 9 years after approval, while biologics selected for price negotiation will be implemented 13 years after approval.

It is estimated that 10's - $100's of billions of future profits could be wiped out based on the passing of this law alone. Industry trade groups like PhRMA and big pharma have pushed back on the IRA citing its potentially negative impact on drug innovation, given the billions in future profits that could be wiped out as a result. It is unclear how this will all shake out, but generally this will put negative pressure on demand for CRO/CDMO services should the price controls lead to a slowing of investment in future

innovation.

Enhanced Government Oversight of Mergers

Over the past year, the US Federal Trade Commission (FTC) and Department of Justice (DOJ) has signaled deeper scrutiny of merger activity in the pharma industry which could slow down or halt certain mergers going forward. In the US Omnibus Spending Package passed in 2022, increased filing fees for M&A will be used by FTC and DOJ to increase enforcement actions in mergers deemed anticompetitive. The fees went into effect in 2023.

As part of the increased scrutiny, the FTC and DOJ may consider changes to how they define "anticompetitive behavior" for pharma which will extend beyond competition as it relates to specific drugs or therapeutic indications. They are also considering to review mergers that span across markets, as well as impacts on future innovation. Scrutiny could also extend to clinical trial design, drug delivery and how platform technologies could have wider applications in field beyond what they are currently being used for.

One high profile example of enhanced scrutiny is Amgen's merger with Horizon which was halted in May 2023 with a lawsuit filed by the FTC. The case against Horizon and Amgen did not hinge on claims of competition (current or future), but rather focused on the possibility for Horizon's blockbuster drugs to be included in Amgen's rebate program. In a settlement on September 1, 2023, the FTC dropped its case and the merger was allowed to proceed.

Implications for CRO/CDMO's:

Price Controls and the IRA – Potential to Decrease Demand for Services: Increasing government pricing controls generally puts downward pressure on CRO/CDMO demand since the fuel for innovation in new therapeutic development has largely come from profits from commercial drug sales. This ultimately impacts negatively on future demand for pharma services.

Increased Government Scrutiny of Mergers – Neutral Effect on Services: Increased government scrutiny on mergers can cause more uncertainty, slow down the process, and cost billions to litigate which is money/resource not spent on pharma services and innovation. On the other hand, the true intent of anticompetition laws is to help foster an environment of diverse innovation and competition which can have a positive impact on demand for pharma services.

Regional Capacity and The On-shoring Conundrum

In last year's CPHI Annual Report, we reported that the on-shoring phenomenon had been maintaining the momentum gained from the pandemic due to additional geopolitical concerns surrounding Russia/Ukraine, China/Taiwan, and growing political tensions between the US and China. In the past 12 months, those concerns have been dampened somewhat, and generally speaking, the momentum towards on-shoring seems to have lost some steam. While on-shoring continues to be a significant topic for discussion, with few exceptions our conversations with many CRO/CDMO's in the US and EU have not revealed widespread evidence to support a consistent and material increase in business attributed to on-shoring. This is particularly true in our discussions with smaller pharma services companies, and those participating earlier in the drug development process. Hyperbolic talk of widespread on-shoring does not seem to match the reality on the ground. Why is this?

The current on-shoring climate is really a battle of competing forces. Those forces that originally ignited the supply chain re-alignment surge (Covid, Geopolitical tensions, other risk mitigation) have been partially offset by calming geopolitical tensions, easing supply chain disruptions, and the current funding challenges prompting renewed focus on cash management (ie re-considering lower cost regions for outsourced services). There is also the realization that disentanglement from off-shore sources such as China is exceptionally complex, and many supply chains ultimately lead back to China-made raw materials.

In spite of this apparent softening in the on-shoring rhetoric, a recent report from Cytiva (*2023 Global Biopharma Resilience Index*) cited just under half (44%) of pharma leaders feel that their supply chains are more robust than they were one year ago, and only 19% of pharma executives say that increasing supply chain resilience is a domestic priority for the next two years.

What is clear from this report is that if supply chain realignment (on-shoring) is going to systemically take hold, there needs a sustained, long-term industry and governmental prioritization to create a climate that supports such a complex initiative. Otherwise it ebbs and flows with the political cycles.

CRO/CDMO Valuations and the M&A Climate

CRO/CDMO's have generally seen valuations continue to modulate over the past year, but appear to be at, or near a trough (Figure 9), and flattening out around levels seen just prior to the pandemic which is about 20-25% below the peak

seen in 2021. TTM July 2023 shows only marginal declines in public valuations versus 2022.

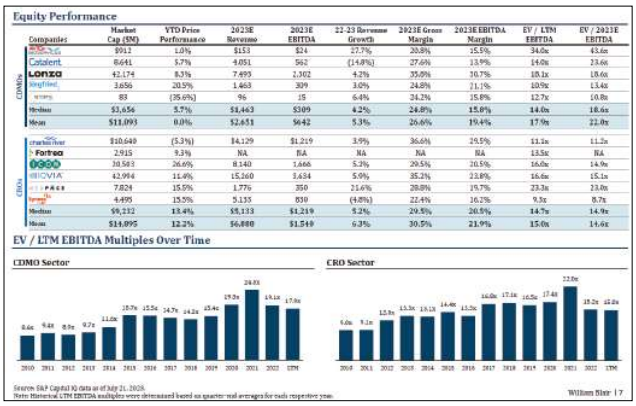

Figure 9: William Blair Equity Research, Pharma Services Update, July 2023

According to Bain Capital's Global Private Equity Outlook 2023, private equity managed to post its second-best year ever in 2022, riding a wave of momentum coming off the industry's record-breaking performance in 2021. However, inflation and related interest rate hikes caused a sharp decline in deals, exits, and fund-raising in the second half of 2022.

The number of private equity healthcare services platform deals (LBO's) saw a steep decline starting in Q4 2022, extending through Q1 2023, and modestly picking back up in Q2 2023 (Figure 10). Interestingly, according to KPMG (Biopharma Services Update H1-2023), while overall PE deal counts are down, the sector has continued to witness strong participation from the private equity community as nearly 68% of all M&A deals were PE-backed. This level is consistent with the level seen in 2022 70% and represents a marked increase from the 2019 (pre pandemic) level in which 44% of transactions were PE-backed.

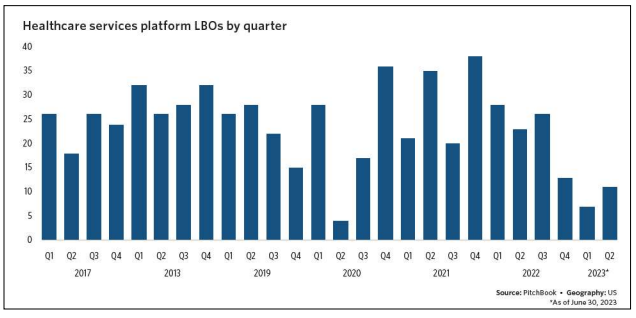

Figure 10: Pitchbook H1-2023 US PE Mid-market Report

It should be noted that while there has been a significant decline in the number of deals executed in the past three quarters, the amount of PE dry powder continues at historically high levels and the need to deploy capital remains high. However, given the broader economic landscape, and dampening valuations, sellers continue to sit on the sidelines awaiting for the right time to go to market. We have heard consistent feedback from the investment banking community that they expect deal volume to pick up later in 2023 into 2024. This will coincide with continuing improvement in biotech funding/valuation climate, and a stabilization/improvement in inflation and interest rates.

Summary on the Health of the CRO/CDMO Sector

The long-term demand drivers for the pharma services sector are strong, driven by strong pipelines of both small and large molecules across the entire drug development cycle, and a macro environment that favors more outsourcing. However, since last year's CPHI the CRO/CDMO sector has gone through a period of realignment. While pandemic and geopolitical pressures have subsided, inflation, higher interest rates, a capital supply/demand imbalance in emerging pharma, and a clogged IPO funnel have marshalled in a period of softening demand for services generally across the industry. Resultantly, emerging pharma generally have migrated towards cash preservation mode. There are signs of an improving VC funding environment, but this needs to coincide with increasing pharma M&A and a more healthy IPO environment. We believe softer demand, particularly from emerging pharma and in earlier phases of development, will extend for a period of 12-18 months.

Concurrently, CRO/CDMO valuations have modulated a bit, but appear to be stabilizing at levels prior to the pandemic (versus the highs of 2021). PE-backed deals and exits have slowed in the sector due to market conditions and buyers waiting on the sidelines. Noteworthy is that PE is participating in nearly 70% of the deals getting done, and the investment banking community is signaling a pickup on deal activity likely starting late 2023 into 2024.

Additional Questions and Answers

Are market forces and outsourcing costs now likely to be the main trend in the next 18-months – i.e. 'putting a pin' in the much talked about reshoring for now?

"With capital somewhat tight at emerging pharma now, there has been a shift towards more cost containment and limiting cash burn. We are hearing from CRO/CDMO's that this had manifested itself in the form of: 1) more scrutiny on proposal pricing; 2) limiting scope of proposals to smaller milestones before releasing future phases of work; 3) emerging pharma focusing spend on fewer programs."

Similarly, with a more stable geopolitical environment (compared to China [and the recent

Canada/Trudeau issues aside]) is India the likeliest CRO/CDMO 'winner' of the recent macro trends for the next 18-months?

"Yes, we have been hearing from both western and Indian CDMO's that the on-shoring momentum in India has been particularly consistent and strong over the past couple of years. That consistency has not been felt as much in the Western regions."

Both Catalent and Lonza have had fairly negative press around their most recent growth figures and CEO changes. Yet in the latter case some growth (4%) was recorded – do you think the largely negative reaction was perhaps overblown, or is it indicative of potentially falling sales in the next 12-months and this what the market is really about warning (falling share price)? (i.e. weakness in early stage outsourcing as alluded to in your article).

"Again, the long-term fundamentals for CRO/CDMO's are excellent given the number of compounds sitting in all phases of development, and continued market dynamics that favor increases in outsourced penetration rates in the coming years. The current funding/IPO climate in the emerging pharma has to sort itself out which will be a near term challenge over next 12-18 months."

Do you think the next 12-18 months perhaps represent a period of excellent value buying for CDMOs – particularly for biologics CDMOs, which until recently were trading at very, very high multiples. With emerging biopharma now 67% of pipelines and nearly 50% of R&D drugs now biologics does this points to excellent growth for these firms in the medium term?

"Yes, there are very good growth prospects for these firms in the medium term which will help keep valuations strong. For good quality CRO/CDMO businesses coming to market, I'm not sure we'll see value buying opportunities either. Public CRO/CDMO trading comps have shown some softening in valuations over the past 12-18 months, and private company valuations have softened a bit as well, but generally speaking both public and private firms are still trading at relatively high multiples versus historical levels. Many business owners have continued to sit on the sidelines this past year waiting for the right opportunity to go to market. Because the number of actionable M&A in CRO/CDMO is down somewhat, there is scarcity value in those deals that have come to market, and good quality assets have maintained good multiples."

Question about Figure 4: Piper Sandler & Co. September 2023

Looking at the data for this year to date (of $30.2bn for Q1/2) we are on course [if this rate continues] for a year end figure of above $50-60bn, which is equal to or slightly in excess of 2019 figures [even when accounting for inflation]. Data like this is nearly always lagging (see central banks are most often behind the economy as an example) so can you envisage a 2024 with a return to the normal/increasing funding pattern ahead – i.e. $50+bn in biotech funding?

"Yes it does appear that private biotech funding has effectively bottomed out at around 2019 levels which is a good sign. I think many were looking for where the floor would be, and it seems that we are at that point. The IPO environment and pharma/biotech M&A also need to show continued improvement before we know what the new normal looks like in the sector."

When would your estimate be on when the 'record levels of PE dry powder' are released – do you think we might see a trigger event [just a hypothetical example e.g. a change of presidency and a reversal or partial reversal of IRA] or will it just be a reflection of gradually returning confidence?

"Generally speaking there will likely be a gradual increase based on continued signs of confidence in the macro environment. Business owners have been more hesitant to go to market during the past 18 months which has led to fewer deals. We are hearing from the investment banking community that activity level is likely to pick back up 2024 based on their pitch volume and the number of known deals sitting on the sidelines."