KIN+CARTA

Investor Report 2020

Pharma Ecosystem 2020: Trends and Opportunities

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Executive Summary

This report provides insights to help CEOs and Investors accelerate digital value.

The healthcare landscape has been changing at speed for the past decade.

Increasingly digital-savvy consumers. A growing need across an ageing demographic. Dramatically improved technologies and access to services. These changes are not trends that come and go: they are only accelerating, resulting in demand for digital solutions, targeted treatments and care services.

Add to this dramatically increased competition in drug markets, which has opened up a need for support services to optimise the entire drug development process. Doing more, faster, better is the name of the game here - from forays into nascent markets such as NASH[1], to Rare Diseases and new frontier cancer treatments (e.g. CAR-T[1]), to efficiencies in clinical trial and manufacturing processes.

Kin + Carta
Pharma Ecosystem Growth Trends

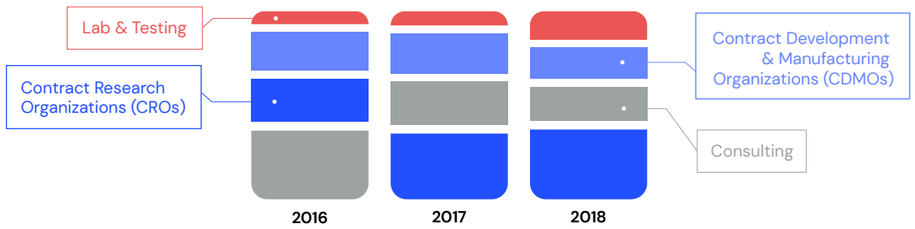
To support these evolving and high-pressured needs, the pharma sector has increased its reliance on outsourcing partners and new innovations.

Investors and entrepreneurs have responded accordingly, and within the pharma ecosystem, consolidation and innovation are looked to for growth acceleration. M&A deal volume across the pharma outsourcing partners is growing, highlighting the interest in this space. 63 transactions were recorded in 2018 vs 57 in 2017 [see transactions by service category].[2] Both the CDMO (Contract Development and Manufacturing Organizations) and CRO (Contract Research Organisations) spaces have seen significant consolidation from an investment standpoint. M&A has unified over 15% of the CDMO market under the five largest companies and 33% under the top five CROs.[3,4]

By creating large one-stop-shops for these services, longer-term contracts are more easily secured driving sticky revenue. To drive further growth beyond consolidation, these businesses are now looking to acquire MedTech and AI innovations to improve their services as well as partners to facilitate their expansion into niche and nascent marketplaces for the development of new treatments.

[1] NASH (nonalcoholic steatohepatitis), is a chronic liver disease relating to the build-up of fat in the liver and is projected to become the primary cause of liver transplantation in the next 10 years. Estes, C. (2018). Modeling the epidemic of nonalcoholic fatty liver disease demonstrates an exponential increase in burden of disease. Hepatology. 67(1): 123-133.
[2] A type of treatment in which a patient's T cells (a type of immune system cell) are changed in the laboratory so they will attack cancer cells. https://www.cancer.gov/publications/dictionaries/cancer-terms/def/car-t-cell-therapy
[3] Capstone Headwaters Analysis https://capstoneheadwaters.com/sites/default/files/Capstone%20Headwaters%20Pharmaceutical%20Outsourcing%20M&A%20[1]Coverage%20Report_Q1%202019.pdf
[4] Pharmatimes Feature on CROs http://www.pharmatimes.com/magazine/2019/march/the_rise_of_the_cro
[5] CDMOs offer a series of services (beyond manufacturing) to assist pharmaceutical sponsors in the stages of manufacturing, for example, analytical development, stability of drug tests and drug optimisation. CROs provide clinical research support, for site selection, patient enrolment or project management capabilities. CMOs offer manufacturing services to support the delivery of small capacity clinical trials, to large scale commercialisation quantities. The CMO (Contract Manufacturing Organisation) market, exposed to similar market pressures, however, has remained highly fragmented, likely as they represent a combination of players large and small that are complex to knit together.

Transactions by Service Category



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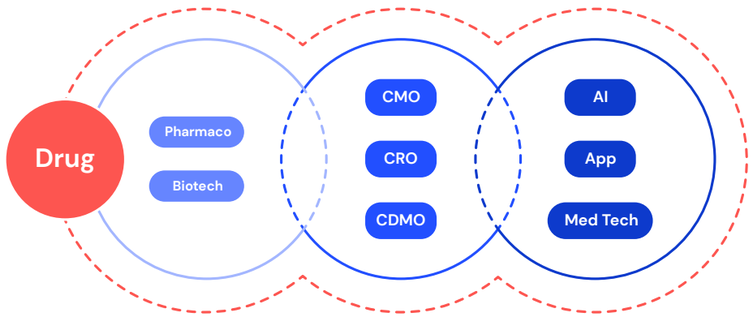
Advances and investment in digital health is growing at an incredible rate, predicted to register a CAGR of 28% from 2018-2024,[6] and many new technologies are not merely consumer-facing. From wearables, to apps, to digital platforms, the data and efficiencies generated by these innovations are opening up important avenues across the pharma ecosystem. As pressure on improving drug development heats up, data, digital and technological innovations are critical to delivering the desired business and patient outcomes.

The Pharma Ecosystem



The entire pharma ecosystem is evolving, responding to both push and pull factors driving market growth and opening up new investment opportunities as these trends come together.

Push – New Markets and Speed to Value: there is a need to move into new underdeveloped treatment areas to create value and generate profit via new treatments as old ones go off patent or compete for increasingly smaller share. This requires more sophisticated clinical trials, patient recruitment, and data management. There is also a desire for improved business processes, speed, and efficiencies that large pharma is not agile enough on its own to deliver.

Pull – Desire for Transparency and "Patient as Consumer" trends: data privacy concerns have mounted and consumers are no longer happy with the status quo 'Black Box' relationship they have with pharma companies perceived to be using their data for financial gain. The trend of 'patients as consumers' has increased expectations in terms of experience, support services, and treatment efficacy, with minimal impact on their quality of life.

[6] Capstone Headwaters Analysis http://capstoneheadwaters.com/sites/default/files/Capstone%20Headwaters%20Pharmaceutical%20Outsourcing%20M%26A%20Coverage%20Report_Q1%202019.pdf
[7] https://www.gminsights.com/

Key-Takeaways

1. M&A across the outsourcing partners has resulted in a consolidated CRO market whilst fragmentation remains across the CDMO and CMO space. The focus for growth, however, has shifted to business efficiencies and specialty avenues to optimise profit margin.

2. The increase in R&D for targeted treatments and rare diseases means that CROs and other support services that underpin drug development and diagnostics will be key investment targets going forward.

3. AI will not only be important for molecule identification, but it will also play a major role in optimising clinical trials (by improving participant recruitment processes and retention) and speeding up time-to-market for new treatments (by facilitating the recruitment of the right patient populations, drugs will have a better chance of both endpoint success and trial completion).

4. Wider data, digital, and technological advances can most effectively tackle the major problem of patient retention for clinical trials. Enabling less complicated participation in trials as well as offering access to trial participation from home (without need to travel to a specific trial site) will greatly improve participation rates - and as a result - drug development timelines.

Outsourcing the ecosystem

In today's fiercely competitive market, with growing costs, quality and efficiency pressures, it isn't a surprise that pharma is looking to outsourcing partners to shore up drug development needs.

Although these relationships have existed for many years, the pressure on CDMOs and CROs to optimise their offer is more acute than ever before. Increasingly stringent regulations, growing complexity of clinical trials, and highly specialised drug manufacturing and distribution requirements mean quality partnerships are more critical than in years gone by.

These outsourcing partners are specifically looking to data, digital and technological improvements to gain a competitive edge. Operational improvements that can drive efficiencies for pharma clients are not only attractive, but necessary, as jostling for business heats up. Added to this, is the need to build capabilities in more niche areas, such as rare diseases, where pharma looks to unlock new markets and new revenue streams.

[8] Contract Research Organisation (CRO) Services Market Forecasts to 2024, https://resultshealthcare.com/wp-content/uploads/2019/07/CRO-sector-MA-drivers-and-market-trends-Results-Healthcare.pdf
[9] The Pharma Trends You Need to Know: A CDMO's Perspective, Anil Kane, https://www.wateronline.com/doc/the-pharma-trends-you-need-to-know-a-cdmo-s-perspective-0001
[10] https://www.pharmamanufacturing.com/articles/2019/cdmo-trends-drug-development-and-industry-consolidation/

"[We are seeing] the continuation of the trend for large pharma to consolidate and divest their internal manufacturing capacity, and move towards an outsourcing model for non-core activities".[12]

Kevin Cook, CEO at Sterling Pharma Solutions

The CDMO Solution

Market conditions continue to favour CDMOs, with record levels of investment supporting the pharma ecosystem's growing needs.[8] Outsourcing to CDMO companies has been steadily increasing over time, matching the rise in volatility and costs associated for pharma. In part, this trend is due to the reduction of manufacturing facilities across pharma, as well as the increased reliance on the more efficient services provided by CDMOs. The efficiency improvements are clear: less waiting between R&D projects and faster time to market for a drug means less wastage and better margins. The specialised knowledge, tools, and processes that CDMOs can offer to do this are invaluable resources for pharma companies.

As a result, the past five years have seen roughly 50% of new drugs manufactured by CDMOs, emphasising the significant reliance big pharma has on these partners.[9] Looking ahead, the space is predicted to grow to $1.5 trillion by 2023.[10]

The increasing diversity of CDMO solutions works to meet the needs of evolving customer expectations. This in particular includes the targeted treatments in oncology, and the rare disease space - critically in the spotlight as a major growth area.[11] Innovations in data, digital, and technology along the drug development pathway are the next frontier for improved services that CDMOs can offer.

[11] CDMO trends: Drugs development and industry consolidation, Executive Vice President of Corporate Development, Recipharm, https://www.pharmamanufacturing.com/articles/2019/cdmo-trends-drug-development-and-industry-consolidation/
[11] Roundtable: discussing trends in contract manufacturing, Pharmaceutical Technology, https://www.pharmaceutical-technology.com/features/featureroundtable-discussing-trends-in-contract-manufacturing-5819662/

CDMO Business Model

Definition: CDMOs are looking to develop the first 'end-to-end' business model whereby a single CDMO provides the entire series of services necessary to take a drug from preclinical through clinical studies and post-approval production.

Aim: The aim of these organisations is to assume the third party role of manufacturing the drug across the entire supply chain for a specific product. As stated by VP of CMC Development Valdas Jurkauskas from Akebia Therapeutics, "There is a certain appeal of the potential to simplify the manufacturing and distribution network, reduce sponsor's resources demand, accelerate development, and control the cost".[12]

Benefits: Many of the benefits revolve around the capacity of the third party facilities, specialised knowledge, capabilities for regional regulatory/language complexities, and the fact that sponsors no longer have to invest significantly in their own facilities and innovations to manage late-stage clinical production efforts.

The CRO Linchpin

CRO relationships have become an essential part of modern drug development. Pharma outsourcing to CROs has experienced strong growth over the years, driven by the need for partners that can deliver increasingly complex clinical trials. Now, expectations are even greater, with the need for support in rare diseases and niche therapeutic areas as well as for innovative and efficient services more broadly. CROs that deliver specialised regional activities such as patient enrolment, market research, and market access services have the greatest margins.[13]

With accelerating pressure on pharma companies to speed up drug to market timelines whilst generating cost efficiencies, the CRO market is poised to reach US$41 billion by 2020 (5.4% CAGR between 2017-2020 and accounting for 60% of all drug development).[14]

After the significant consolidation we have seen in this space, current trends within the market indicate that small to medium-sized CRO businesses offer the greatest potential for growth. These smaller firms are demonstrating that they have the agility and the dexterity to create and innovate in order to better meet the needs of sponsors.

[13] Straight talk: end-to-end CDMO and CMO business Models, https://dcatvci.org/6042-straight-talk-end-to-end-cdmo-cmo-business-models
[14] Contract Research Organisation (CRO) Services Market Forecasts to 2024 https://resultshealthcare.com/wp-content/uploads/2019/07/CRO-sector-MA-drivers-and-market-trends-Results-Healthcare.pdf
[15] Contract Research Organisation (CRO) Services Market Forecasts to 2024 https://resultshealthcare.com/wp-content/uploads/2019/07/CRO-sector-MA-drivers-and-market-trends-Results-Healthcare.pdf

The Demand for CMO Agility

The CMO space has demonstrated the greatest agility in changing market conditions. It is the most fragmented of the three (vs. CDMO and CRO spaces), yet has shown rapidly expanding capabilities that directly address evolving customers needs. CMOs have been particularly adept at delivering rare disease and personalised treatment drug manufacturing services. A comprehensive review conducted by Mordor Intelligence stated that the *"biggest factor driving the growth of CMOs in the pharmaceutical industry is the growing need for state-of-the-art processes and production technologies, which have proven highly effective in meeting regulatory requirements."* [15] Combining onerous regulatory processes with intense market pressure necessitates the implementation of innovations that data, digital, and technology can offer. Such optimisation has propelled the industry forward, facilitating its ability to respond to diverse client needs, underpinning CMO growth.

A range of factors are behind the growing importance of CMOs within the production line for drug development. Certainly the digitisation of the supply chain and services that extend beyond many in-house capabilities, are key drivers of success. With increasing consumer influence over price, quality, and service, pharma companies require a strategic CMO partner for the benefit of delivering capabilities most mid-sized pharma companies cannot afford to deliver in house.

An ever-shifting regulatory environment

Changing regulations across countries and regions continue to add cost, complexity and challenges to drug development. No doubt, these exist for the benefit of the patients, but constant changes have a ripple effect across the pharma ecosystem, adding a further burden on health systems, pharma companies, and their outsourcing partners.

- The influence on GDPR on CRO databases looking to fulfil clinical trials with relevant patient groups has presented an administrative, operational, and practical barrier for timely execution and completion of clinical trials.
- Internal compliance measures (and associated increase in resources) have been strengthened for pharma and outsourcing partners alike to respond to stricter regulations on data privacy, security, and fair-use. Weighty fines are now a reality to warn against data leaks or breaches.
- A fundamental shift is taking place in the regulatory framework for medical devices with the Medical Devices Regulation (MDR) from May 2020. More strict regulations for approvals will be in place and appropriate certification for medical devices in the UK and EU will be required as a result. This initiative is anticipated to have a significant (negative) impact on device development and approval timelines, as well as approval success rates.[16]

Navigation through the regulatory nuances and changing goalposts is no easy feat. Pharma companies rely on a whole host of partners across the ecosystem to facilitate and advise on the most effective steps to take. This need for specialist advice underlines the importance of high-quality partnerships and high expectations in this space.

[16] Pharmaceutical Contract Control Development and Manufacturing Organisation (CDMO) Market Growth, Trends, and Forecast (2020-2025), https://www.mordorintelligence.com/industry-reports/pharmaceutical-contract-development-and-manufacturing-organization-cdmo-market
[17] https://www.meddeviceonline.com/doc/the-european-mdr-impetus-impacts-and-current-status-0001

Leveraging data, digital, and tech to drive success

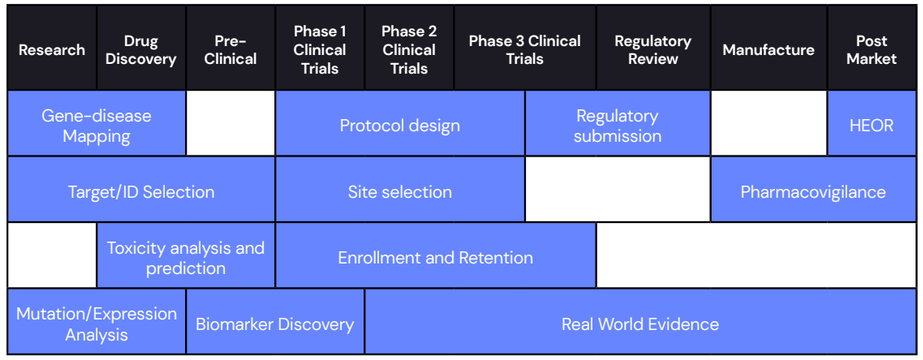
The range of auxiliary offerings across outsourcing partners is gaining great attractiveness. Avenues of specific growth are present primarily because of increased investment, onerous regulatory complexity, and the urgency to tap into unmet patient needs and unaddressed therapeutic areas ahead of industry-wide personalisation efforts. Innovation is looked to for competitive advantage as differentiation disappears.[18]

In addition to competitive advantage, data, digital, and technology is being turned to to address the increasing regulatory burden so that it does not impede business operations and cause delays to drug development timelines. The wider health technology industry is predicted to be worth $280bn by 2021. From flexible costing structures to streamlined internal facility management, there is extensive value to be gained from innovations that can help bring products to market in a decreased time.

One of these avenues is artificial intelligence (AI) which has revolutionised the Medtech space over the past decade and is expected to reach $6.6bn by 2021.[19] AI has the power to deliver the necessary data and digital innovations that promise to answer key pharma, patient, and practitioner needs, at speed.

With a widely available range of data collecting and sharing devices, the age of AI is likely to drive biopharma research out of the laboratories and into our homes. Data (and valuable consumer insights) will no longer be siloed in facilities or servers. It will be accessible, measurable,

AI assistance in the drug development process



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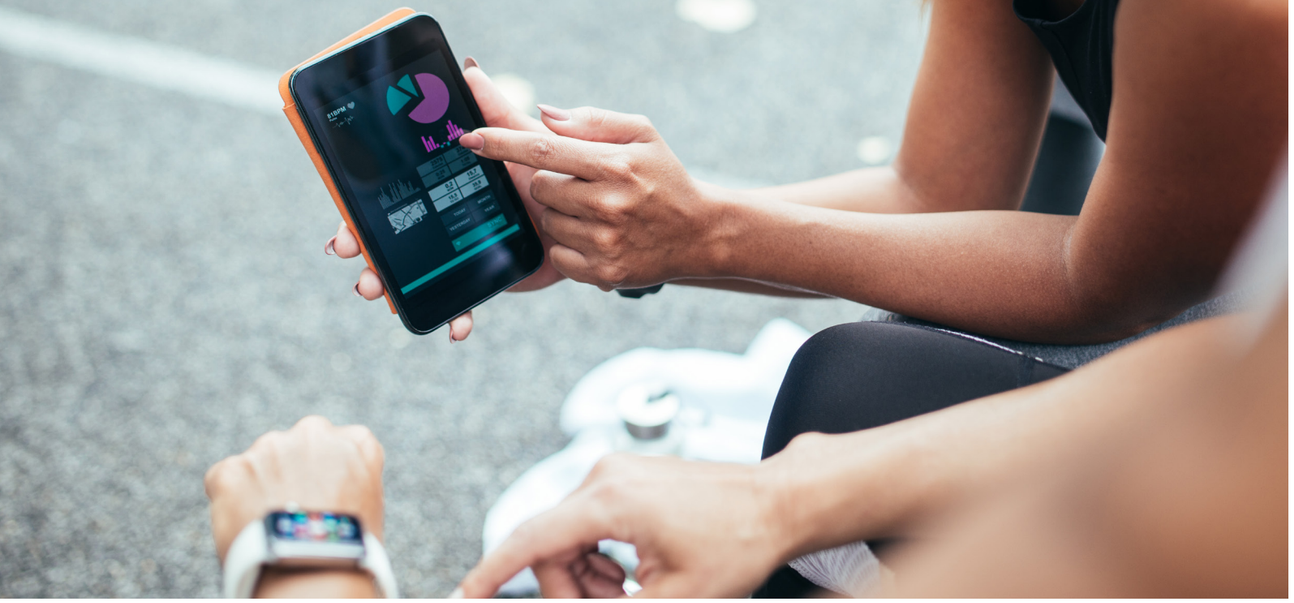
and comparable to millions of other data points of patients globally, generating a robust and comprehensive understanding of patient welfare and treatment outcomes. Medtech innovation and AI adoption will likely be the primary solution for shortening clinical trials and driving more successful trial results.[21]

Within the CRO and CDMO sectors, AI offers a distinct competitive advantage to clients. Clearly, it has the potential to generate significant cost efficiencies whilst speeding up time to development through innovations across the board.[22]

[18] CRO Industry Primer – The Evolving CRO Value Proposition, Erin Wilson, Robert Willoughby, Mark Wallach, Credit Suisse, https://plus.credit-suisse.com/rpc4/ravDocView?docid=IRNadZ
[19] Contract Research Organisation (CRO) Services Market Forecasts to 2024, Researchandmarkets.com, 2024 https://resultshealthcare.com/wp-content/uploads/2019/07/CRO-sector-MA-drivers-and-market-trends-Results-Healthcare.pdf
[20] https://capstoneheadwaters.com/sites/default/files/Capstone%20Headwaters%20HCIT%202019%20Year%20in%20Review%20Coverage%20Report%20.pdf
[21] Contract Research Organisation (CRO) Services Market Forecasts to 2024, Researchandmarkets.com, 2024 https://resultshealthcare.com/wp-content/uploads/2019/07/CRO-sector-MA-drivers-and-market-trends-Results-Healthcare.pdf
[22] An AI boost for Clinical Trials, Marcus Woo, Nature, https://www.nature.com/articles/d41586-019-02871-3



Key advances

Accessibility and retention

One of the most significant barriers to clinical research is appropriate patient recruitment.[23] A staggering number of clinical trials fail as the result of unsuccessful trial recruitment. In cancer trials alone, roughly 25% fail to recruit the necessary number of patients.[24] However, recent advances in AI have begun to offer hope. IBM's Watson, for example, has been shown to improve breast cancer clinical trial enrolment by 80%.[25]

Companies we like

https://www.antidote.me/ ; https://www.ert.com/

[24] Feller S. 2015. One in Four Cancer Trials Fails to Enroll Enough Participants. https://www.upi.com/Health_News/2015/12/30/One-in-four-cancer-trials-fails-to-enroll-enough-participants/2611451485504/
[25] An AI boost for Clinical Trials, Marcus Woo, Nature, https://www.nature.com/articles/d41586-019-02871-3
[26] https://www.ncbi.nlm.nih.gov/pubmed/31342909

Linguistic mapping and pattern recognition

Natural Language Processing (NLP) and the Machine Learning capabilities are working to streamline recruitment workflow.[26] Pattern recognition is being leveraged to solve recruitment delays, lag, and mis-recruitment. This technology means that automated programmes screen in and out patients for trials more effectively than ever before by quickly triangulating recruitment criteria with electronic health records (EHRs). It is well understood that drug delays to market can cost up to $8m a day. If NLP can process 10-30 times more patients than manual screening, this can translate into a significant upside for pharma companies.[27]

Companies we like

https://www.linguamatics.com/ ; https://www.trinetx.com/nlp/

Wearable data

AI has the potential to revolutionise the collation of data. There is considerable difficulty attributed to clinical trials, monitoring, and patient feedback which even now, is only steadily being overcome with Real-World Data and profiling. Early findings[28] suggest that the introduction of wearables mitigates the risk of missed intelligence, serves as a reminder for key milestones such as taking tablets, and provides real-time information to be sent automatically, reducing the need for patient travel to medical appointments or the need for patient-HCP interactions.

Companies we like

https://www.careology.health/ ; https://www.iconplc.com/

[27] Clinerion's Patient Recruitment https://www.clinerion.com/dam/jcr:2d621c5b-259d-4aca-8195-fd03dbc6e928/CIC%20Healthcare%20Briefing%20Note%20Clinerion%20Final%202016.pdf
[28] Wearables benefits https://www.welbi.co/single-post/5-health-benefits-of-wearable-tech

Robotic Process Automation

The early adoption of Robotic Process Automation (RPA) will streamline supply-chain, administrative functions, and patient scheduling, allowing doctors to spend more time with patients and offset the risk of human error. On the supply chain side alone it is estimated that RPA can reduce downtime by 30-40%, boosting overall equipment effectively and driving tangible benefits for the business.[29]

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https://www.signavio.com/ ; https://www.nice.com/

"By 2024, organizations will lower operational costs by 30% by combining hyperautomation technologies with redesigned operational processes."

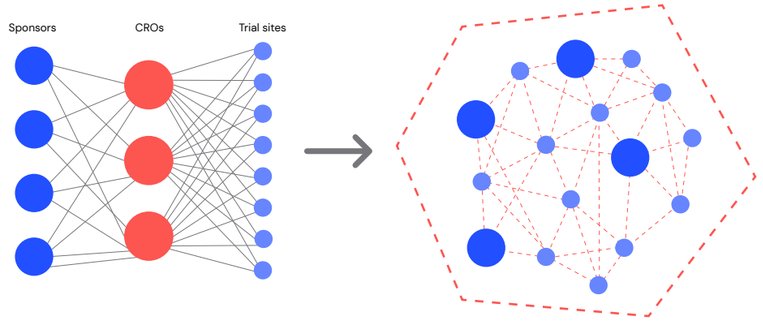
(Gartner Predicts 2020: RPA Renaissance Driven by Morphing Offerings and Zeal for Operational Excellence)

Blockchain

Potentially difficult to action but incredibly valuable, will be the application of blockchain within a healthcare network. A cloud-based system capable of securely storing, editing and recording patient data across millions of datasets for pattern recognition on an unparalleled scale will revolutionise current patient data practices. With 176 million patient records compromised from 2009-2017, there has been a renewed push for patient data strategies central to improved health outcomes as well as collaborative sharing for increased cross reference of patient information.[30]

Companies we like

https://genomes.io/ ; https://www.silvertouch.com/



Current Clinical Trial Ecosystem

Blockchain-based Clinical Trial Ecosystem

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[29] RBA in Pharma https://www.Intinfotech.com/blogs/enhancing-pharma-supply-chain-effectiveness-through-process-automation/
[30] 15 Examples of How Blockchain is Reviving Healthcare, Sam Daley, https://builtin.com/blockchain/blockchain-healthcare-applications-companies
[31] https://www.imperial.ac.uk/business-school/blogs/features/imperial-students-use-blockchain-improve-clinical-trials/

"While we still have a long way to go - the maturation of the devices and the way in which we handle data in terms of both collection and management and of course the regulatory environment - it's clear wearables bring untapped potential to clinical trials, enabling researchers and clinicians to capture data at the point of experience."

Dr. Sam Volchenboum, co-founder and chief medical officer of Litmus Health

Success Criteria and Risk Factors

We have identified five ways in which outsource partners and associated support services/ technology businesses have driven success: differentiating value in line with pharma needs, approach to customer engagement, strong value proposition, and effective digital infrastructure.

1. **Differentiating value in line with future pharma needs:** Outsourcing partners and ecosystem businesses must leverage cutting edge digital, data, and technology to drive competitive advantage to provide Pharma clients with the necessary optimised offer they need to hit increasingly stringent targets.

2. **Modernised approach to customer engagement:** As with the trend towards personalised medicine, so must be the 2020 customer experience, leveraging a range of channels and making the most of digital.

3. **Compelling, quality value proposition:** High quality partnerships are the most desired, leveraging innovations that can deliver pharma speed to market advantage.

4. **Strong digital infrastructure with flexibility to respond to customer needs:** From automated reporting rooted in cutting-edge data-science to innovations that facilitate clinical trial participation, the more data-led tools outsourcing partners have in their toolkit the more successful they will be.

5. **Clear offer:** With all the whizzy new solutions to drive efficiencies and optimise success for pharma clients, outsourcing partners need to be able to articulate this as part of a simple benefit and outcome – focussed offer.

That said, with any new frontier always comes risks due critical consideration. These are five-fold and highlight nuances from data security, to scalability, to geographic, and cultural constraints:

1. There are general risks associated with outsourced manufacturing and supply chain, including data processing, data security, control over timings, and quality assurance.

2. High barriers to entry on the outsourcing front have resulted in a 'lag' of innovation which means there is significant work to do to shift largely analogue businesses into the digital world we are now in; stringent regulations are ever present barriers to such 'digital twin' creation in terms of timelines and feasibility.

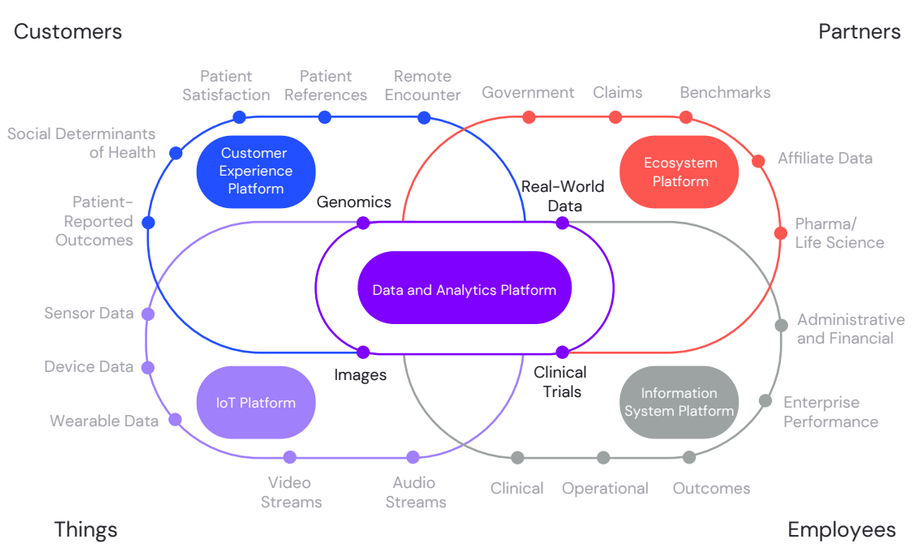
3. Scalability of small-scale AI technology remains unproven in larger scale, highly expensive clinical trials. Incorporating a new approach and technology into clinical trials is a huge risk given the level of investment, time and complexity of each and every trial.

4. Global supply chains are relied upon for large pharmaceutical companies and with this comes the added complexity of geographic, cultural, legal, regulatory and language barriers.

Despite these risks, the pharma ecosystem is established, respected, and relied upon by pharmaceutical companies of all shapes and sizes. The trend for increasing reliance over the coming years is clear.

Contract organisations de-risk pharma investment in drug development, simplify entry into new markets, and operate as strategic partners. New trends in this space suggest that we are ever closer to the one-stop-shop solution, so desired by pharma. With heavy competition and a consumer base with an increasingly loud voice, opportunities for investment and value acceleration across the pharma ecosystem are highly attractive.

Digital Care Delivery Data



Making it Happen

At Kin + Carta, there's a reason we refer to our family of organisations as The Connective.

When healthcare-focused investment and management consultants work alongside product designers, the strategy, vision, and technology necessary to accelerate growth are clear from the start.

When engineering teams sit alongside data scientists and marketing specialists, data can be shared faster, experimentation never stops and new opportunities are uncovered in real time.

We believe that the key to creating lasting change is to put the right people in the room. If you'd like to continue the conversation, our team of specialists is eager to hear from you.

Get in touch today.
We'd love to help you make it happen.

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Pharma Ecosystem 2020:
Trends and Opportunities

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