propharma

Innovation and the black swan

the imperative of AI-enabled clinical research

WE DESERVE THE WIN. The concerted efforts of financial incentives, legislation and expedited approval pathways continues to advance rare and orphan disease R&D. Since the landmark Orphan Drug Act of 1983, we've made significant strides in the pursuit of science and patient health. In 2022, more than half of the drugs approved were designated for rare diseases, signaling a profound alignment between innovators, their investors, and regulators[1].

And collectively, we've earned the win. However, scientific innovation alone didn't get us here nor will it be enough to take us where we want to go. Where policy and financials create a forcing function for scientific innovation, scientific innovation requires an equally relentless pursuit of new enabling tools and technologies. Which in turn creates its own demand from individuals and teams to create and deliver new solutions. Or put simply, innovate.

Innovation is not something that highly regulated biopharmaceutical and medical device industries have traditionally done well. Driven by a focus on building efficient operating models to deliver high quality, consistent results at scale, biopharmaceutical and device companies have not been afforded the opportunity to think deeply about the sources, foundations, consequences, or durability of innovation. However, if 2020's black swan is any teacher, they need to figure it out.

Clinical research organizations (CRO) saw success in the late 20th century and built large, scale-driven businesses to match the period's blockbuster zeitgeist. However, the Orphan Drug Act (ODA) of 1983 changed that. Once largely overlooked by the pharmaceutical industry due to small patient populations and limited profitability of developing treatments, the financial incentives afforded by the ODA increased attention and investment. As blockbuster drugs (drugs with over $1billion) for more common conditions faced patent cliffs and increased competition, many companies and investors have since turned to rare disease as a strategic area of focus. This increased focus has culminated with over 50%[1] of approved products in 2022 having an orphan designation. Which in turn has incentivized a generation of new data and technology solutions that help connect scientific innovation to meaningful patient benefit (Figure 1).

An example can be seen in the early-to-mid 2010's with an explosion of real-world data companies such as: TriNetx (2013), Komodo Health (2014), and Science37(2014) to name a few. These companies provided access to claims data, EMR data and other observational data and framed the real-world evidence narrative; effectively advancing the utility of real-world data to help innovators understand how best and to whom they should develop and market their new medicines.

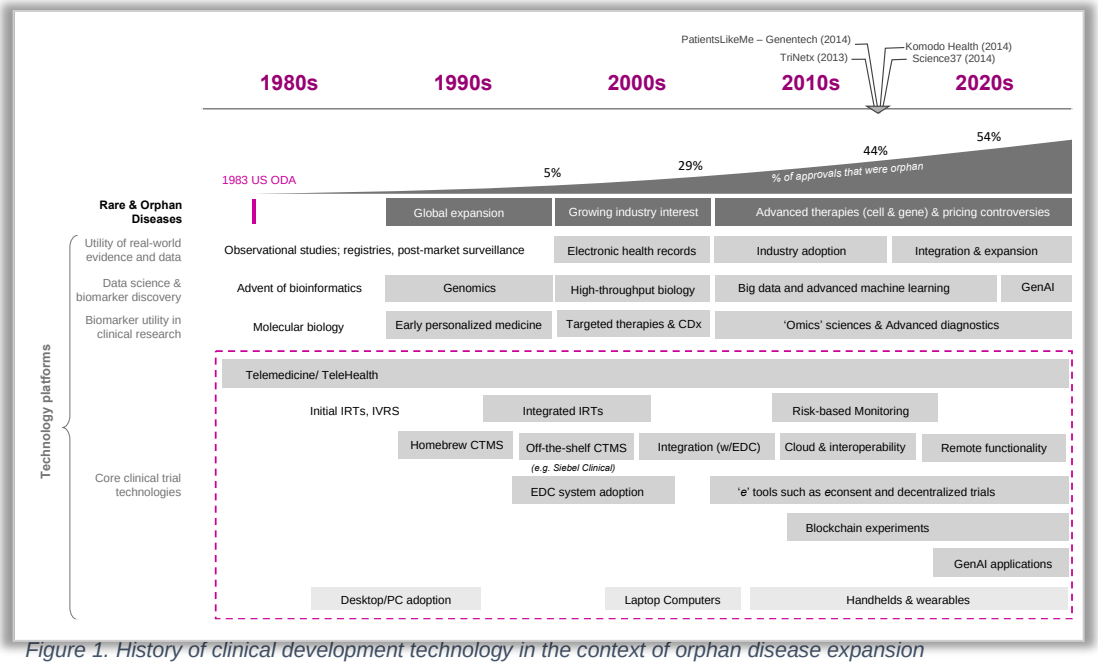


Figure 1. History of clinical development technology in the context of orphan disease expansion

[1] CDER 2023, <https://www.fda.gov/drugs/our-perspective/cder-continues-advance-rare-disease-drug-development>.

Unfortunately, the overall operating model of traditional CRO hasn't fundamentally changed. Still wired for blockbusters, the clinical research outsourcing industry maintains a predictable recipe for success: deliver on the basics, differentiate through either experience or technology, merge for scale, and acquire access to data/new technologies.

However, as Mike Tyson said, "Everyone has a plan 'till they get punched in the mouth." And black swans are just that – a punch in the mouth. The startling events of 2020 were a shock to the clinical research industry, disrupting critical research and exposing weaknesses in traditional research models. Looking back, winners were those companies that were able to quickly transition innovative experiments into primary workflows – a capability that could only have been developed pre-pandemic, where creative engagement across interdependent teams provided an uncommon agility and an inherent capacity for innovation.

Here we review the various dynamics that impact the ability to innovate when getting punched in the mouth and provide a few ideas on how to leverage new technologies to win in a world where all big diseases are increasingly stratified into smaller diseases.

Background

Historically, in a highly operationally focused, highly regulated business environment, individual functions are often rewarded on how well they squeeze inefficiency out of their part of the process. Often acting independently in this pursuit, functions focus myopically on achieving their own incremental gains with little regard for upstream or downstream internal 'consumers'. Events and behaviors that fall outside of the boundaries of each function's responsibilities are someone else's problem or if they occurred within their purview, they would be labeled 'exceptions' – undesirable and seemingly wasteful disruptions to process. Such tight controls provide little room for trial and error, experimentation, and little patience for non-conforming ideas looking to help the organization compete. One can argue that the CRO industry, on the whole, is no exception. Ironically, given the highly competitive and highly commoditized market, it is exactly these creative elements that are required to differentiate for an advantage.

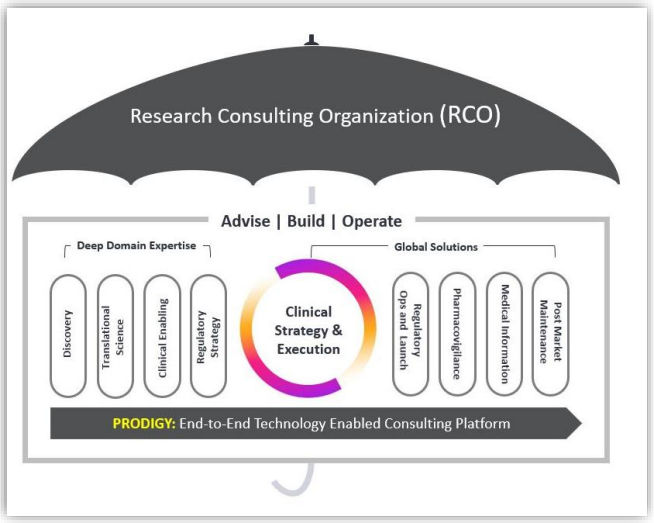
Yes, one can argue that the 2020 pandemic forced a more remote-capable business model, but once patients were allowed back into sites, sites returned to face-to-face interactions as a preferred way to interact with study monitors. Revealing the change resistant, inelastic model that continues to weigh down the clinical research industry. While virtually driven firms are rightly credited with being creative in their pursuit of decentralized solutions and democratizing clinical research, the fundamental clinical research process hasn't fundamentally changed, and broad scale transformation remains elusive.

So what?

Pharmaceutical services companies and CROs now find themselves as members of the knowledge economy. Where the nature of work is not only information-based, but also consistently nonlinear, only partially predictable, networked, interdependent, and increasingly collaborative - it takes partnerships with payers, providers, patients and other new players in the healthcare delivery system (e.g. think Google or Apple) to succeed. A productive business in the knowledge economy is dependent upon information as a core commodity - that information could be data, or it could be stories & content, and in order to thrive our organizations depend on the creation of that knowledge and its role in finding paths to innovation. This stands in stark contrast to the more linear business model of organizations in the past, which focused on repeatable procedures and controlled efficiency that worked fairly well when applied to highly regulated high-volume services or large-scale widget manufacturing.

Our solution: Embrace insights as a foundation for sustainable innovation.

At ProPharma we have built and continue to cultivate insights through a technology-enabled consulting mindset. As the cornerstone of our RCO model, technology-enabled consulting aims to establish a sustainable way of operating that drives innovation and fundamentally helps the industry in its journey from volume to value, where access to information, and the utility of technology and evidence continue to drive increased nuance and opportunity for innovators. This is especially true for those looking to improve patient outcomes and medicinal value by capitalizing on the accelerated pace of democratization, and the increasing volume, variety, and velocity of information (e.g. biomarker discovery tools, AI-everything, etc.). Understanding how and when to engage in the frenzy can be daunting. **At ProPharma we use two governing principles as guideposts: 1) Be the easiest organization to do business with and 2) Be an insights leader.** This interdependence between the enabling technologies that enhance our services and solutions and the culture that uses them is at the heart of our RCO model and has shaped the way our teams leverage technology to provide friction-free and insightful experiences to our clients.



In 2023 alone, ProPharma invested over $5 million USD, to advance **Prodigy** – **An End-to-End Technology-Enabled Consulting platform**, a purpose-built suite of technology-driven solutions that help our industry partners and internal teams to obtain answers to their most critical questions faster, de-risk decision making and ultimately do less with more [data]. Prodigy is comprised of three core capabilities:

1. Artificial Intelligence (AI) enhanced solutions that span clinical development and research, regulatory, medical information, and safety.
2. Informatics and advanced analytics with respect to applied real world evidence, diversity, equity, and inclusion (DEI), and predictive modeling.
3. Productivity via automation of internal/external processes

"Fundamentally, the shift from volume-to-value is about doing less with more [data]. At ProPharma this means keeping pace if not leading the charge into an AI-first world."
-Mike Stomberg, CEO

Intelligence solutions

AI-enhanced solutions use machine learning and other AI techniques (e.g., natural language processing) to improve the performance of traditionally manual intelligence solutions.

Specific solutions we have developed that have benefited from an AI "lift" include site & patient intelligence solutions, label intelligence, health authority decision intelligence and literature search/review. In each case, customers and internal teams have benefited from up to 50% improvements in speed, quality and cost.

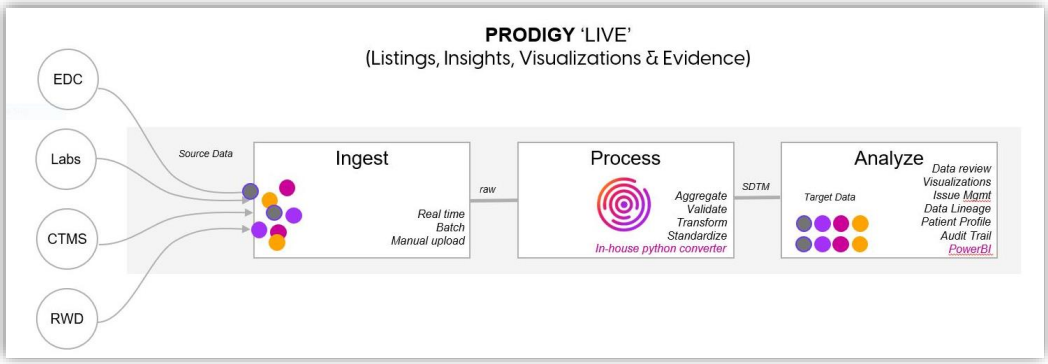
- *Site & Patient Intelligence Solutions* – Identify patients and rapidly surface site performance across ProPharma's site and patient networks.
- *Label Intelligence Solutions* – Cloud-based solution natural language processing and semantic search-based tool that provides automated comparisons and competitive monitoring to inform product strategy and development.
- *Health Authority Decision Intelligence* – AI-enhanced search, extract, and evaluate approval/denial filing precedent with easy access to regulator commentary.
- *Literature Search and Review* - Automated search and screen of publicly available literature in multiple languages

Informatics

Healthcare accounts for 30% of the world's data volume and is estimated to reach a 36% compound annual growth rate (CAGR) through 2025[2]. Given such unprecedented volume and velocity in data creation, ProPharma has committed to and invested in two primary strategies: 1) partner to access massive data and 2) build a proprietary data curation engine as part of our Prodigy platform that ingests, processes, and analyzes data from disparate sources.

While ProPharma generates a significant amount of data from our daily conduct, we also understand the increasing utility of real-world data to shape and advance new therapies. To that end, we have partnered with H1, a leading aggregator of healthcare information. Our collaboration not only allows us to derive critical insights for innovators but also has provided a partner keen to surface insights with AI tools, large language models specifically. The result of our collaboration is ProPharma's ClinCHAT, a natural language GPT interface into H1's significant data stores.

Our in-house data curation and visualization engine, Prodigy 'LIVE', further enables our clients to rapidly, and with high quality, transform raw data from EDC, PK, and labs into an SDTM standard, which is then organized and visualized into automated dashboards and reports.

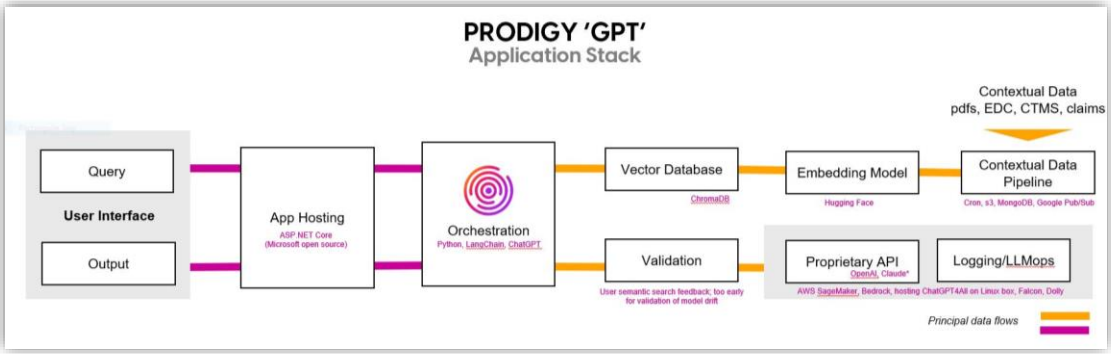


Critically, this approach simplifies access to insights for both clients and staff across all ProPharma's service lines; improving the ability of each of our teams to focus more on the implications of data rather than front end traditionally manual curation activities.

"At ProPharma, AI-first implies democratizing access to these new resources; transforming the fabric of our business and improving the ability of our teams to drive the future of science." *-Mike Stomberg, CEO*

Productivity tools

A core focus of technology-enabled productivity tools is the ability to automate repetitive and mundane tasks. We have applied robotic process automation and AI to free up our teams' ability to focus on more complex, creative, and value-adding activities, thereby increasing productivity and efficiency at both individual and organizational levels. These tools have been particularly useful when applied in a medical writing context – automating the development of patient narratives, patient profiles, and conducting source document quality reviews.



Behind these tools is a large language model construct that enables an advanced level of data analysis and information processing. By consuming vast amounts of text and being able to generate coherent, contextually relevant responses, our Prodigy GPT architecture helps ProPharma and our clients make sense of large data sets, find patterns, generate insights, and make more informed decisions faster. This ability not only reduces the time needed for data processing but also increases the accuracy of results, leading to improved decision-making and enhanced productivity.

[2] RBC Capital Markets: https://www.rbccm.com/en/gib/healthcare/episode/the_healthcare_data_explosion

Creating a new path to value

Ultimately, our objective is to collaboratively work with innovators to surface insights based on whatever data we have access to, e.g. claims, EMR, CTMS, etc., and provide targeted information and evidence to accelerate and de-risk development, articulate a more compelling narrative, and increase medicinal as well as commercial value.

This approach effectively extends our vision beyond the traditional faster-better-cheaper model, allowing us to help our customers build differentiated brands.

Surfacing insights. Semantic Search aims to optimize the extraction of insights from large, disparate databases and simplify access to these insights using natural language. Large Language Models are utilized to leverage the vast array of available insights to their maximum effect, driving creativity and helping innovators connect the dots. Automation speeds up the collection of real-world data to align with real-time technologies, ensuring findings are curated and promptly surfaced for consideration and application.

Clinical strategy. In developing a winning clinical strategy, several elements are crucial: the Story, the Evidence, and the Delivery. The Story aspect involves a clear understanding of product identity/brand and a differentiated value story for investigator preference/case for use. With Evidence, the focus is on acquiring the necessary evidence for reimbursement, both in the US and the rest of the world (RoW) and identifying what additional evidence could help de-risk delivery and accelerate adoption. Delivery entails ensuring the clinical operations strategy is de-risked for patient access, recruitment, and retention, enabling efficient and high-quality data collection, and leveraging KOL/investigator experiences to seed the brand in the market.

Medicinal value (MV). MV is ultimately shaped by efficacy, access, and uptake. Efficacy is evidence provided by the clinical experiment and its sufficiency supporting the new drug or device's claims and therapeutic effect. Access examines if the evidence meets local regulatory requirements and competitive payer formulary placement. Lastly, uptake assesses whether the insights support a value narrative that encourages health care provider and payer interest and usage.

Bottomline…

Embracing AI-enabled tools and technologies is critical to supporting and informing the future of scientific achievement. As diseases continue to become 'smaller' and therapies more nuanced, solving for the volume-to-value transition across the life science industry is critical. To this end, ProPharma has invested in complementary technologies that allows us to flex our delivery models to support variations across innovator size and scope – a hallmark of the RCO model.

Leaning towards an AI-first future is the next frontier for clinical research and the commercial availability of large language models and vector databases has democratized access. These tools, coupled with semantic search, and automation have specifically allowed ProPharma to dynamically help sponsors connect the dots across data, tools, tactics, strategy, and impact and move from transaction-based thinking (e.g. what is needed to get this new drug approved), towards a more end-to-end value-based mindset where being AI-first is being patient-first.