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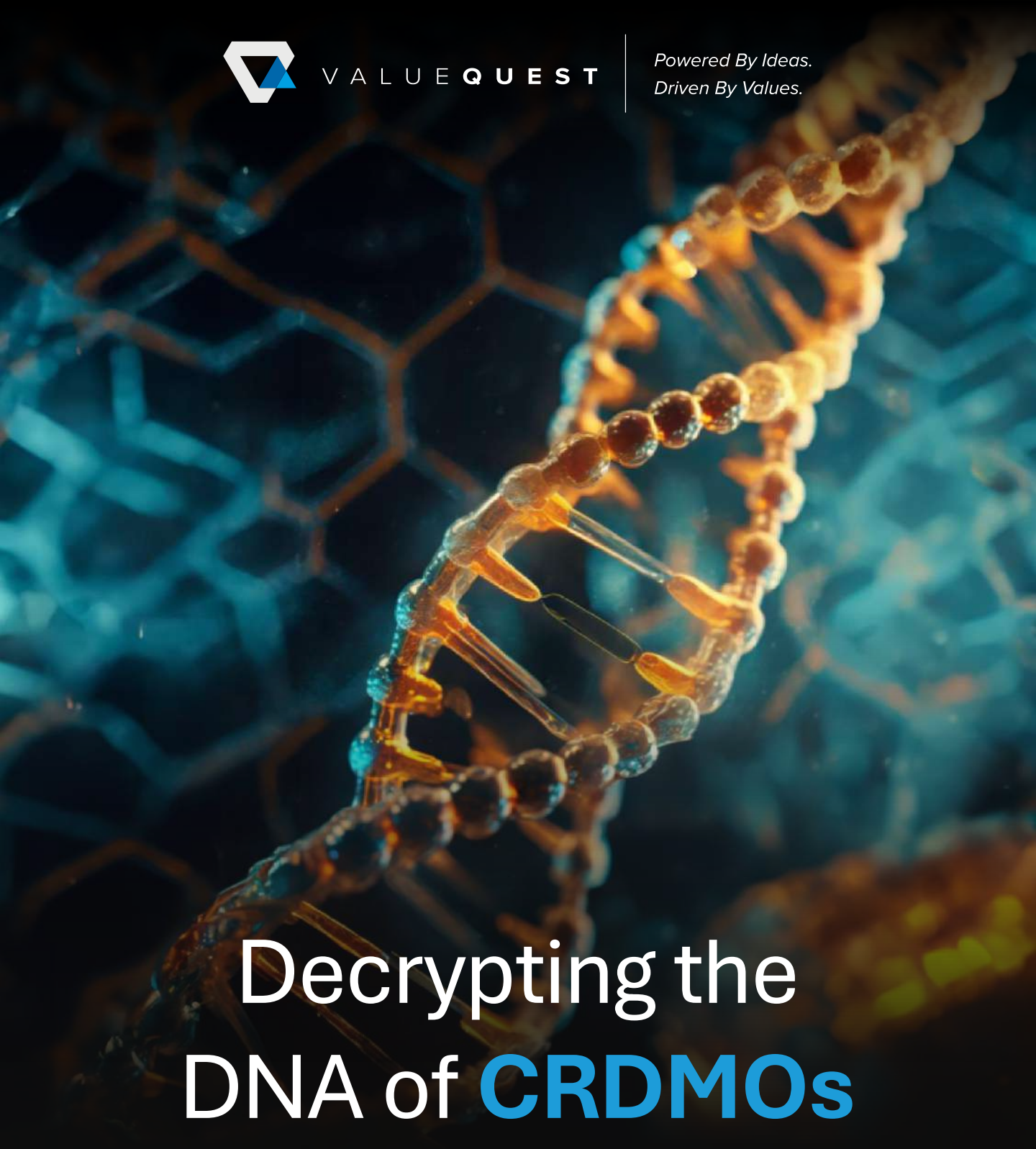

Decrypting the DNA of CRDMOs

VQ Deep Dive

January 2025

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Executive **Summary**

India's pharmaceutical industry has long been a global powerhouse in generic formulations, meeting an impressive 25–40% of the generic drug requirements in regulated markets like the US and UK. However, the story of Indian pharma is evolving, with a growing opportunity to establish itself as a key player in Pharma R&D outsourcing through the burgeoning Contract Research, Development, and Manufacturing Organization (CRDMO) industry.

A New Chapter in Indian CRDMO Growth

While India's current share in the global pharma R&D outsourcing market is less than 5%, the trajectory ahead looks promising. A combination of global supply chain disruptions, the need for diversification by innovators, increasing maturity of the Indian ecosystem, and regulatory support are all creating tailwinds for exponential growth in this sector. However, success will not be uniform across the entire R&D value chain. India has a clear "Right to Win" in select areas:

- **Contract Research Outsourcing (CRO):** India is poised for robust growth in this space, leveraging its cost-efficient scientific research capabilities and abundant talent pool.
- **Small Molecule API Development and Manufacturing:** With multinational innovators actively diversifying away from China, India’s strong API manufacturing capabilities position it as a reliable and cost-effective alternative for small molecules.

In other segments, such as biologics (large molecules) and clinical trial outsourcing, the Indian industry lags global peers. Scaling these areas will require coordinated efforts from the industry and robust government support.

Building an Ecosystem for Leadership

The Indian CRDMO ecosystem is already taking decisive steps to capitalize on the opportunities ahead. Companies are expanding capacities through brownfield and greenfield projects, acquiring niche players with biologics expertise, and improving quality systems and compliance frameworks. At the same time, the Government of India’s Production-Linked Incentive (PLI) schemes and other support initiatives are bolstering the industry's growth potential.

A Differentiated Path to Global Leadership

India’s CRDMO growth story will be driven by a select group of companies with differentiated capabilities and innovative approaches. These "winners" will not only outpace the broader market but also position India as a trusted global partner in Pharma R&D.

The journey ahead is ambitious, but with the right mix of focus, investment, and strategic intent, the Indian CRDMO industry is set to play a transformative role in shaping the future of global pharma.

Outlay of the Newsletter

Pharma R&D
is a Long and Risky Journey

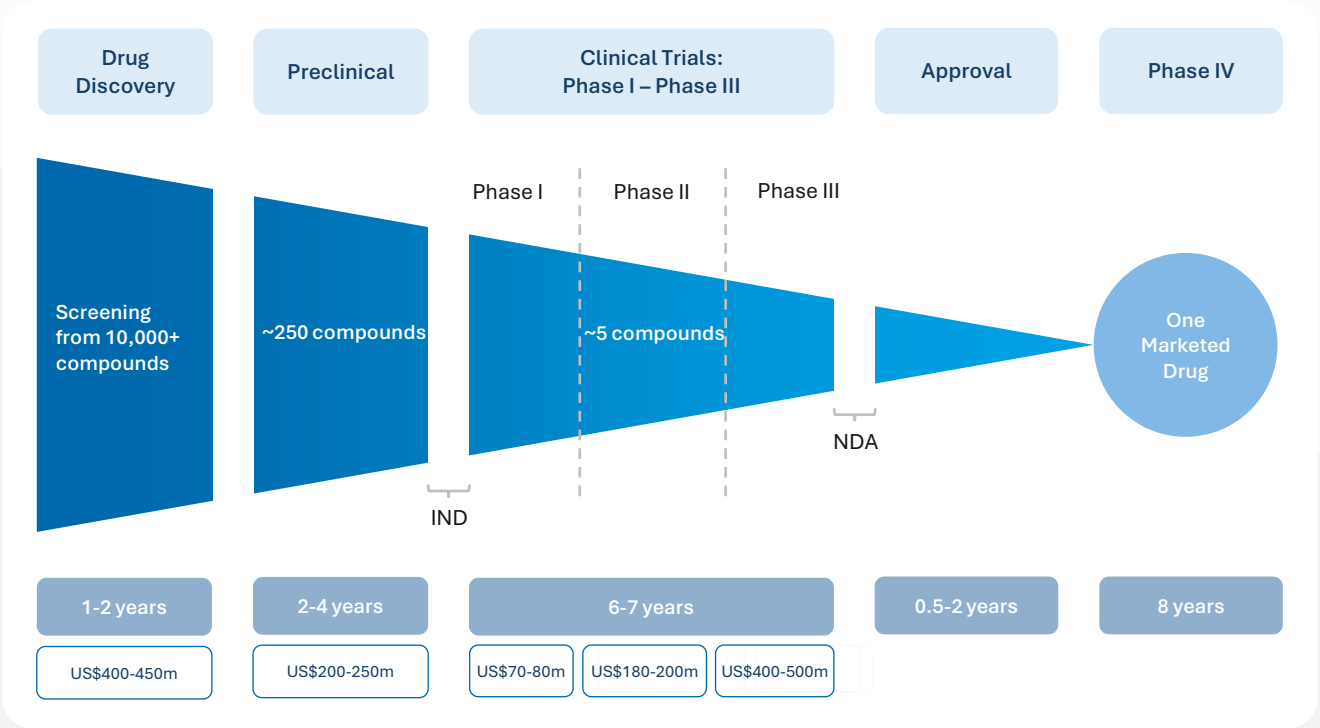
01

The pharma R&D value chain starts with developing compounds (chemical or biologics) in the laboratory and then testing their efficacy against a particular ailment at three levels—laboratory, animal, and finally, human trials. A new drug needs to go through extensive testing and regulatory review at each stage to examine and verify its safety and efficacy before it is approved for market release.

Therefore, the entire process, from the discovery stage to commercialization, is time-consuming and takes several years due to the vast amount of data that needs to be collected and analyzed before moving to the next stage. On average, the process typically takes more than 10 years.

Moreover, the success rate is low when progressing from one stage to the next, as compounds can affect the human body in ways that are difficult to predict at the laboratory stage.

Chart 1: The Pharma **R&D Value Chain**



Sources: Wuxi AppTec, CLSA, Valuequest

The process is also costly, as each stage requires several hundred million dollars to complete. On average, it costs USD 1.5–3 billion over the entire duration of 9–12 years.

Furthermore, the success rate for developing a new drug from discovery to approval is extremely low at less than 0.01%. Only a small fraction of experimental drugs, ranging from one in 10,000 to 15,000, successfully progress from preclinical trials to regulatory approval and commercialization.

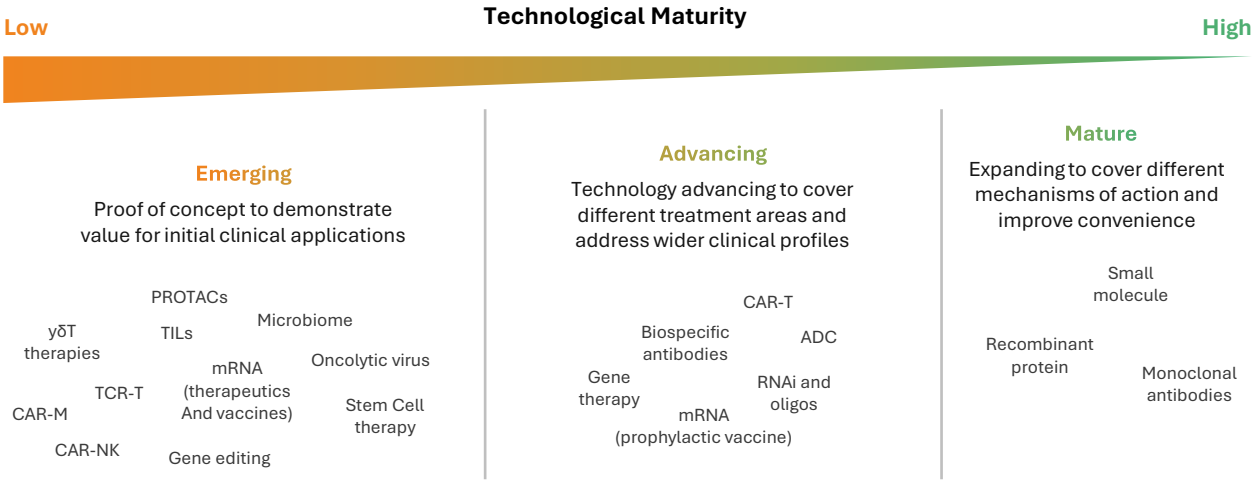
Drug Development Faces **Complexity** and **Rising Costs** 02

In Terms of Drugs

Learn more about **Chemicals** & **Biologics**

In last 10 years, **advances in technology**, synthetic methodology, and new areas of biology **have opened more opportunities for innovative and creative biologics drugs**. Modulating RNA splicing, stimulating specific types of stem cells, and developing drugs with antibody or peptide conjugates, are just a few examples. **The below chart** emphasizes the progression of therapeutic technologies in terms of maturity, showcasing a shift from emerging concepts to advanced and established treatments with a growing number of applications in the pharmaceutical landscape.

Chart 2: Drug Development Trends



	Other emerging modalities	Stem cell therapy	Oncolytic virus	Biospecific antibodies	mRNA vaccine	Gene therapy	RNAi/ oligos	CAR-T	ADC	mAb	Recombinant protein	Small molecule
Marketed products	0	66	4	3	8	17	18	19	42	140+	500+	37,000+
Global pipeline (early-stage activities)	300+ (99%)		252 (92%)	333 (92%)	76 (97%)	713 (94%)	537 (92%)	682 (96%)	577 (85%)	3,300+ (82%)	xx	14,000+ (81%)

Sources: Evaluate Pharma, BCG

Hence, **a majority of incremental R&D spend is towards Biologics** using **emerging technologies** such as Anti-Drug Conjugates (ADC), Cell and Gene Therapies (CGT), Oligonucleotides, RNA/DNA, etc.

According to a recent Frost & Sullivan report on CRDMO industry, **the biologics market** (at 35% of total pharmaceutical market by revenue in 2023) is forecasted to reach USD 752.1 billion by 2028, from USD 480.0 billion in 2023, **at a CAGR of 9.4%, faster than overall pharmaceutical market.** This change will be driven by increasing adoption of innovations such as immunotherapies, antibody-drug conjugates, and gene and cell therapies.

Within small molecules, R&D spend is mainly happening in areas of High potency APIs. High potency APIs use precision targeted medicine, needing a much lower dosage administration and volume to treat the same diseases. This is against the existing usage of small molecules with a one-size-fits-all approach.

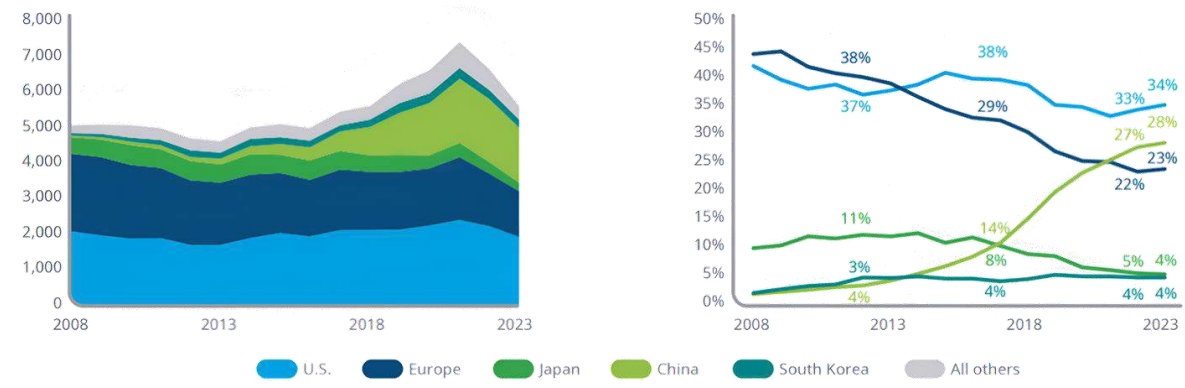
In Terms of Therapies

4 major therapies dominate the R&D efforts of the pharma ecosystem – **Oncology *(cancer)*, Neurology *(central nervous system related ailments)*, Endocrinology and Metabolism *(Diabetes, Obesity, etc.)*, and Immunology *(Immune system)***. Around 80% of the total clinical trials happening in the space are related to drugs which attempt to solve for unmet needs in these therapies. Oncology related R&D has seen strong growth in last 10 years, with an increasing focus on innovative mechanisms of action. Neurology has seen significant growth in trials (to 500+ over last 5 years) to treat neurodegenerative, neuromuscular, and psychiatric disorders. The largest share of trials in neurology remains that of Alzheimer's and Parkinson's diseases. Metabolic/endocrinology include diabetes, obesity and NASH have had a near doubling of number of trial activities around weight loss drugs in last 5 years (focused majorly on GIP/GLP glucagon receptor agonists).

In Terms of Geographies

Pharma R&D spending is mostly driven by **USA** and **European companies.** In absolute terms, **they account for >60% of total R&D spends** and clinical trials. Prominent R&D innovation hubs in USA include Boston, Cambridge, Massachusetts, New Jersey, New York, and Chicago. Other prominent R&D hubs across the world include Manchester, London, Cambridge, etc. in UK, Paris in France, top cities in Japan and Switzerland. Interestingly, post reforms, **China is also emerging as an innovation** hub in recent years.

Chart 3: Number of Phase I to III trial starts based on company headquarters location, 2008-2023

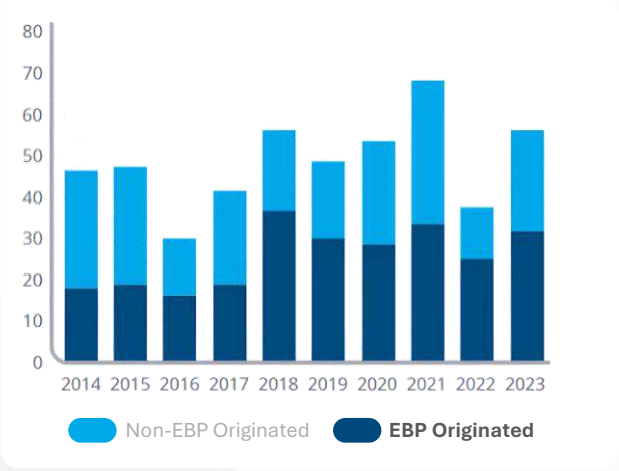


Source: *IQVIA Global Trends in R&D 2024*

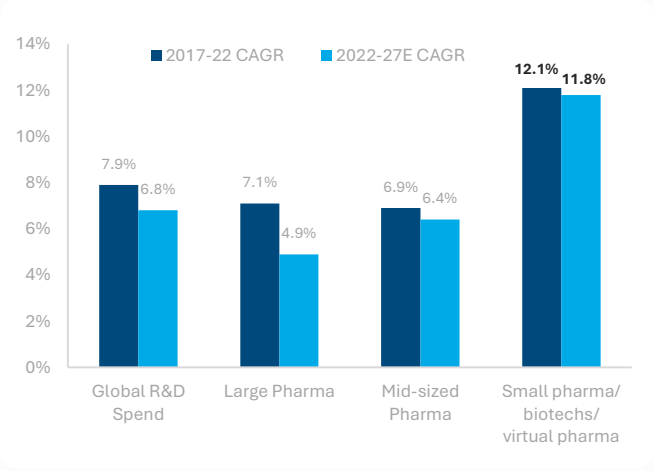
In Terms of Company Size (revenue)

In the last 15-20 years, emerging biopharma companies (small innovators) have seen a meaningful growth in the overall R&D product pipeline. According to IQVIA, emerging biopharma (EBP) companies accounted for **73% of late-stage research** in 2018, compared to 50% in 2003. Moreover, **84% of all early-phase research** was conducted by emerging biopharma in 2018. These firms conducted 65% of all clinical trials and have more trials underway than large pharmaceutical companies across all phases. The number of molecules being developed by EBP has also been increasing annually over the past few years. In 2018, there were ~ 8,700 products or programmes in active development, ranging from discovery to registration, of which EBPs developed **80%**. Since these firms operate on a lean cost structure and rely on external funding to run their R&D programs, they do not have their own facilities and outsource practically most non-core functions to CROs and CDMOs.

Chart 4: Number of New Active Substances by company type 2014-23 & Past and Future CAGR of R&D, Pharma



Source: IQVIA Global Trends in R&D 2024



Source: Frost & Sullivan

Other Areas of R&D

A rise in complexity of design and development of drugs also implies more steps in manufacturing which in turn necessitates more innovation in manufacturing processes. The aim of process R&D is to improve unit productivity, enhance product quality, reduce lead times and lower capital and operating costs.

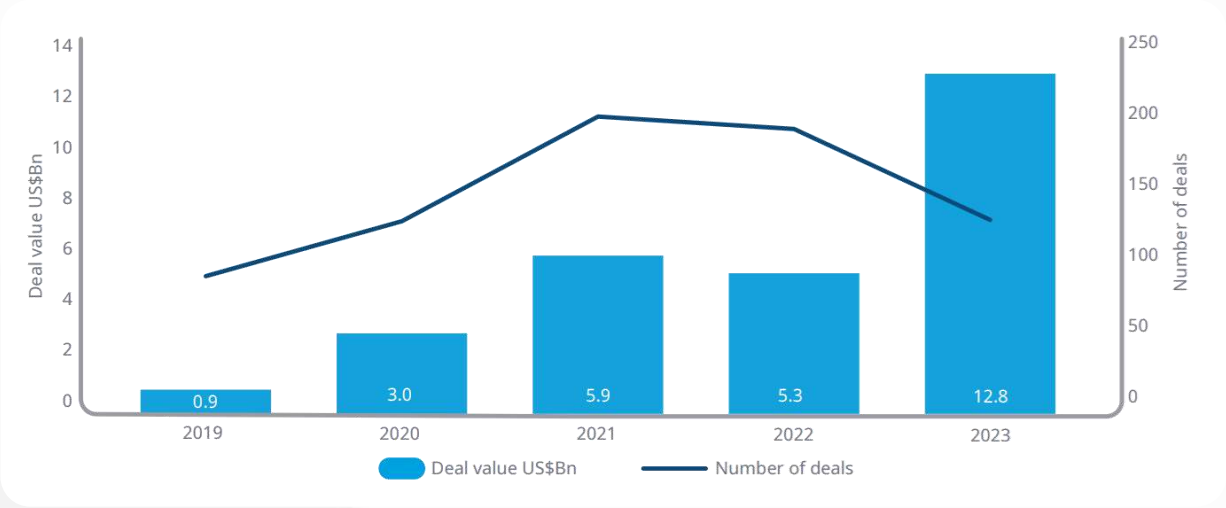
Several new technologies have emerged in recent years to improve the quality, consistency, and efficiency of products while reducing the need for labour. Some of the prominent new technologies used in manufacturing of pharma products include – **continuous flow manufacturing, single use manufacturing, automation, particle engineering, newer alternative materials, innovations in capsule design and packaging, electroporation / nucleofector technology,** etc.

These technologies introduce modularity in manufacturing to provide batch size flexibility (scale up / down capability through different stages of testing & commercial production.

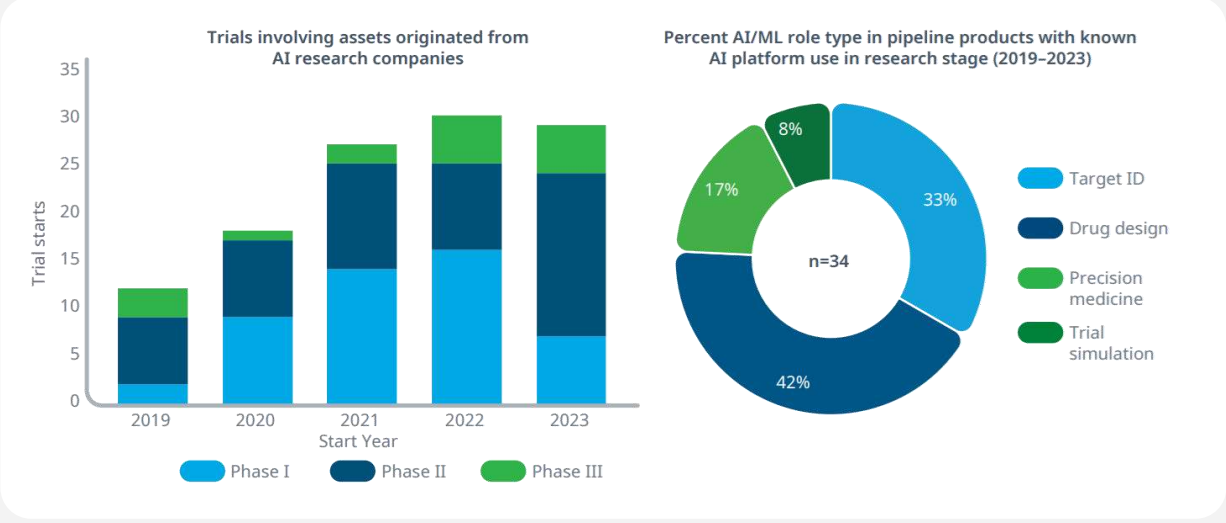
Use of Information Technology

All of this is backed by the increasing use of software and tools such as data analytics, Artificial Intelligence (AI), Machine Learning (ML), etc. for drug discovery and patient cohort identification. 2021 saw **100+ drug and biologic application submissions using AI technologies**. Recognising its importance, USFDA released a paper in May 2023 for stakeholders to discuss the use of AI/ML in drugs and biological product development. The proof of the pudding is in the fact that the last few years have seen several large multi-billion dollar deals occurring in this space with large pharma companies acquiring AI-based pharma innovator companies.

Chart 5: AI/ML Contribution to the Pharma Industry



Source: IQVIA



Source: IQVIA

Rising R&D Costs Create **Challenges** and **Speed Bumps** 03

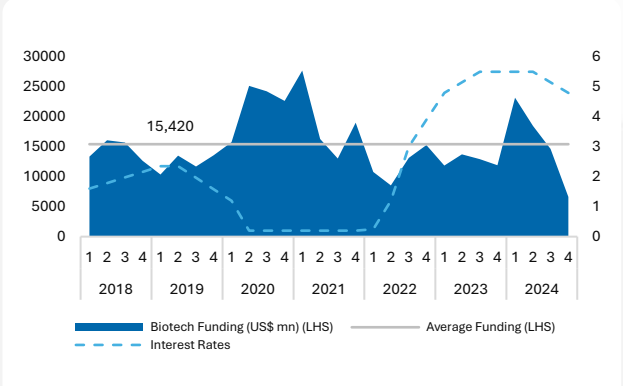
Pharma R&D spend is being driven by emerging biotech innovators in USA and Europe to solve unmet clinical ailments with the use of latest generation drug modalities and manufacturing technologies.

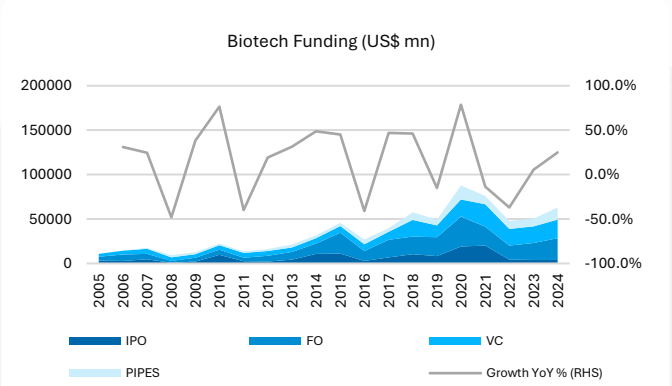
Most of these innovators are start-ups founded by small scientific teams who have novel concepts in mind but not the financial resources to carry out the expensive drug development activities. Thus, they are dependent on external funding to take them from concept to commercialisation. A **lack of budget and funding has been one key reason for the slowdown in R&D activities** in the past. Regulatory hurdles or lack of scientific activities are not the detractors here. In the past, **3,000+ compounds have been shelved because of lack of funding**.

Angel investors and Venture Capital are most critical to early-stage start-ups whereas **PE and listed M&A investments are mostly directed towards late-stage companies** who have a few molecules in phase 3 trials. This is where the macro interest rate environment plays a key role. **Lower and stable interest rate environment is most conducive to biotech funding.**

Recent quarterly trend reflects the challenges as well as volatility in the funding environment, driven in part by higher interest rates across the world leading to higher cost of funding. **However, when looked on longer time frames, funding has started to pick-up again which should augur well for improvement in R&D spend.**

Chart 6: Funding has started to pick-up again which should augur well for R&D spend improvement





Source: *VQ, Jefferies*

However, more importantly, capital providers are being increasingly choosy about which projects they fund.

The environment is characterized by haves and have-nots. New molecule identification has taken a backseat with slow movement in early stages of the life cycle. Timelines have increased from RFP stage to the project awarded stage. Innovators are taking time between and within stages to evaluate the risk-reward at various points.

The ones who have a clear inexpensive path to the next milestone (those in late-stage Phase 2 and 3 trials, with good clinical data and outcomes from previous rounds, having high-conviction molecules) are able to raise oversized capital rounds.

This is leading to fewer but larger deals in the space. Even then, deployment is slower than before. Innovators are quick to forego further stages if data or outcomes do not show the requisite positive signals. This has lead to higher drop-out rates and moderation in clinical trial starts. This is most evident in the M&A environment where large pharma companies are acquiring promising innovator companies having a few molecules with good P2/P3 clinical trial outcomes for billions of dollars (with most of them in areas of Oncology and Neurology).

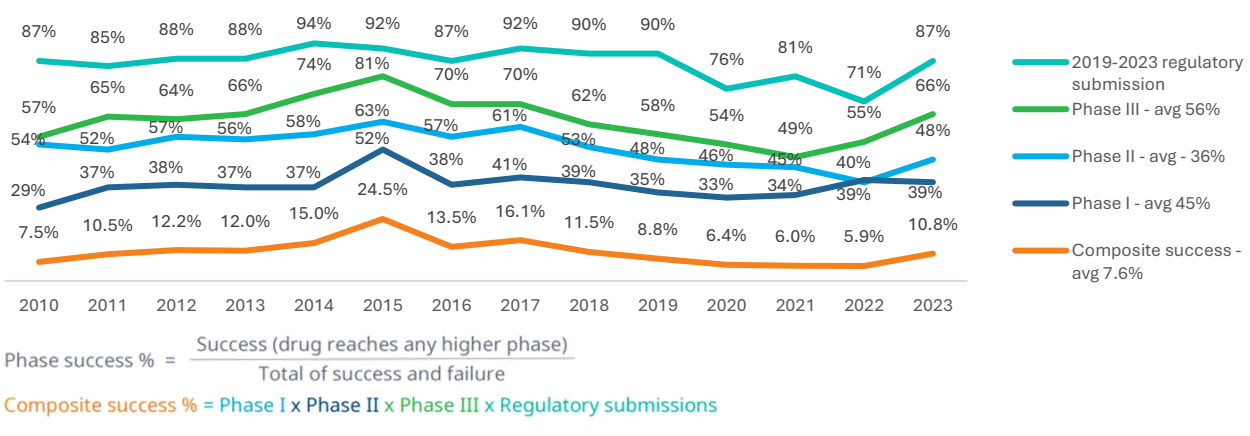
Innovators Incur Higher R&D Costs

Pharma R&D pipelines have grown at ~8% CAGR over the past 5 years, reaching ~20,000 molecules by CY23. However, new commercial launches have remained flat at ~55 annually, reflecting a poor success rate. Success rates have declined from 0.5% in 2018 to ~0.3% in CY23, with drops seen across therapies, drug types, company sizes, and discovery phases (source – Frost and Sullivan).

Key reasons for the poor success rate include -

1. **Rising Increasing complexity of drugs being developed and therapies**
2. **Increasing complexity of trials which must take into account multiple factors** *(number of subjects, eligibility, countries, sites, age group, availability, etc.),* **and**
3. **Increasing duration of trials at various stages**

Chart 7: R&D composite success rate and average phase success rates Phase I to filing, 2010–2023



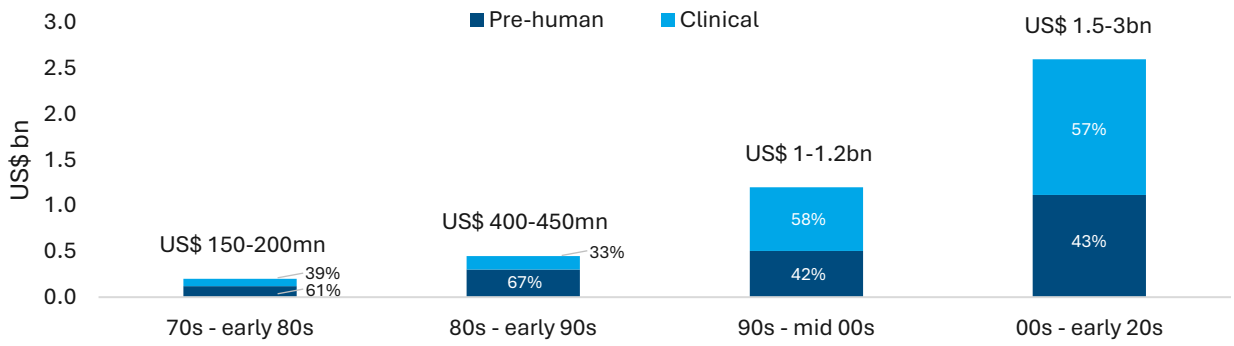
Source: *IQVIA*

Thus, the R&D process is time-consuming, capital-intensive and risky. The success rate of developing a new drug from drug discovery to approval is extremely low, and if failure risk is taken into account, average R&D costs of a marketed innovative drug may reach USD 3-4 billion, according to Frost & Sullivan.

The cost of developing a new drug has doubled every 9 years since 1950. The average cost to develop and commercialize a new drug today (R&D to marketplace) is nearly USD 3-4 billion, a 10x increase since 1970s. **Money spent developing just one successful drug today is equivalent to the cost of developing 90 drugs in 1950s**, even after adjusting for inflation. Timelines from drug discovery to commercialization have more than doubled from an average of 6 years in the 1970s to 13-14 years in the 2010s.

The last 2-3 years saw a modest reduction in R&D cycle times and a decline in average cost of developing a drug as industry adopted some novel trial designs and made improvements in efficiency through digitization of drug discovery and development. Overall, returns on R&D investment have been on a decline for innovators.

Chart 7: R&D cost per approved drug



Source: *Goldman Sachs*

Apart from the extended timelines and complexity, the cost of manufacturing and complying with regulations has also risen in innovation hubs and nearby regions. The cost of scientists and production workers in these geographies has become increasingly prohibitive.

CRDMOs **Streamline Costs** and **Accelerate Progress** 04

Investing in creating their own capacity for every stage of R&D is a risky move as innovators may have only 2-3 molecules at the commercial stage. This leads to significant cash burn in initial years and eventually creates sub-optimal IRRs and ROCEs over the entire lifecycle. With a surge in R&D costs, long cycles, and low success rates, there is increasing pressure from investors on pharma companies to generate returns on their R&D investments. Innovators are increasingly focused on cost control and efficiency improvement.

Contract Research Development and Manufacturing Organisations (CRDMOs) are organizations that offers contractual services to innovators to help develop and manufacture drugs. They take up some of the innovators' non-core work relating to the initial R&D stages, late-stage clinical trials and manufacturing activities. They can do the same faster and with more efficiency.

Chart 8: CRDMOs Vital for Innovators at Various Stages

Stage	Drug Discovery	Preclinical Development	Clinical Development	API Manufacturing	Drug Product Manufacturing	Packaging and Supply Chain	Commercial Manufacturing	Post-Marketing Surveillance
Innovator Roles	Discover and design novel molecules	Conduct preclinical studies for safety & efficacy	Sponsor & design Phase I-III clinical trials	Oversee process development for proprietary APIs	Develop proprietary drug formulations for delivery	Ensure compliance with regulatory packaging and labeling	Oversee technology transfer and production scalability	Monitor drug safety and efficacy in the market
	Invest in R&D technologies and early-stage research.	Design drug candidates for clinical trials	Ensure regulatory compliance	Ensure high quality and regulatory compliance	Oversee quality & consistency	Manage supply chain logistics	Ensure adherence to global regulations	Develop life cycle extensions for existing products
CRDMO Roles	Assist with early-stage synthesis and biologics screening.	Manufacture preclinical trial material (small quantities: APIs/ biologics)	Produce clinical trial materials (APIs/formulations)	Manufacture APIs at various scales	Provide formulation development	Provide packaging (primary & secondary) and serialization	Scale-up for large volume production	Support new formulations or delivery methods
	Provide specialized platforms for discovery		Support process development and scale-up	Offer specialized tech (e.g., continuous manufacturing)	Manufacture finished drug products (oral, solids, injectables, biologics)	Handle global logistics and cold chain management	Offer lifecycle management support (e.g., biosimilars, new formulations)	Continue manufacturing of mature products

Sources: *CLSA, Jefferies, ValueQuest Internal Research, Industry Sources*

As is evident from the above pictures, CRDMO help innovators at various stages of the value chain in a variety of ways.

CRDMO companies are mainly classified into 3 types:

1. **Clinical Research Organisation (CRO)**
2. **Chemistry Manufacturing and Control (CMC) / Contract Development and Manufacturing Organisation (CDMO)**
3. **Contract Manufacturing Organisations (CMO)**

CRDMOs are one-stop service providers who can provide full value chain services ranging from drug discovery to commercial manufacturing. They are the most integrated of the 3 types.

Outsourcing to CRDMO helps innovators in several ways:

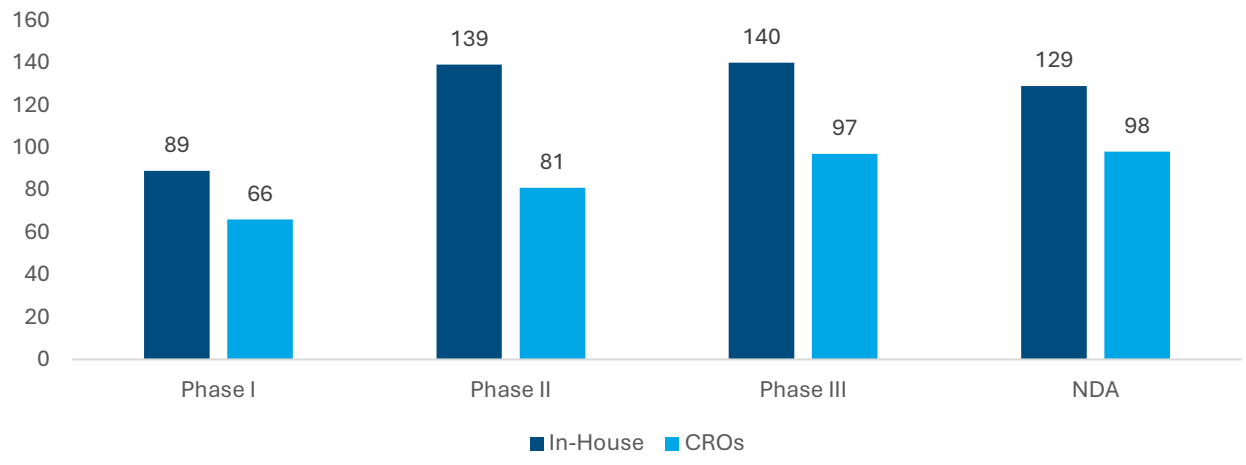
1. Converts a portion of their R&D budgets from an upfront fixed cost to a variable cost

Outsourcing reduces R&D intensity for innovators and allows them to operate more efficiently, thereby reducing the financial burden for innovators. With outsourcing, innovators can invest their limited capital into core R&D while outsourcing capital intensive non-core ancillary and supplementary work to CRDMOs. Thus, a share of their R&D budget (upfront fixed asset investments and non-core operations) is reduced considerably and converted to a variable cost. This gives them the flexibility to shift strategic and development priorities in response to market conditions.

2. Reduced R&D timelines

CRDMOs help reduce overall timeline by 0.5-1 year which is a significant number in the context of overall R&D costs and success rates.

Chart 9: R&D timelines (in weeks) reduced significantly with CROs



Source: *Jefferies*

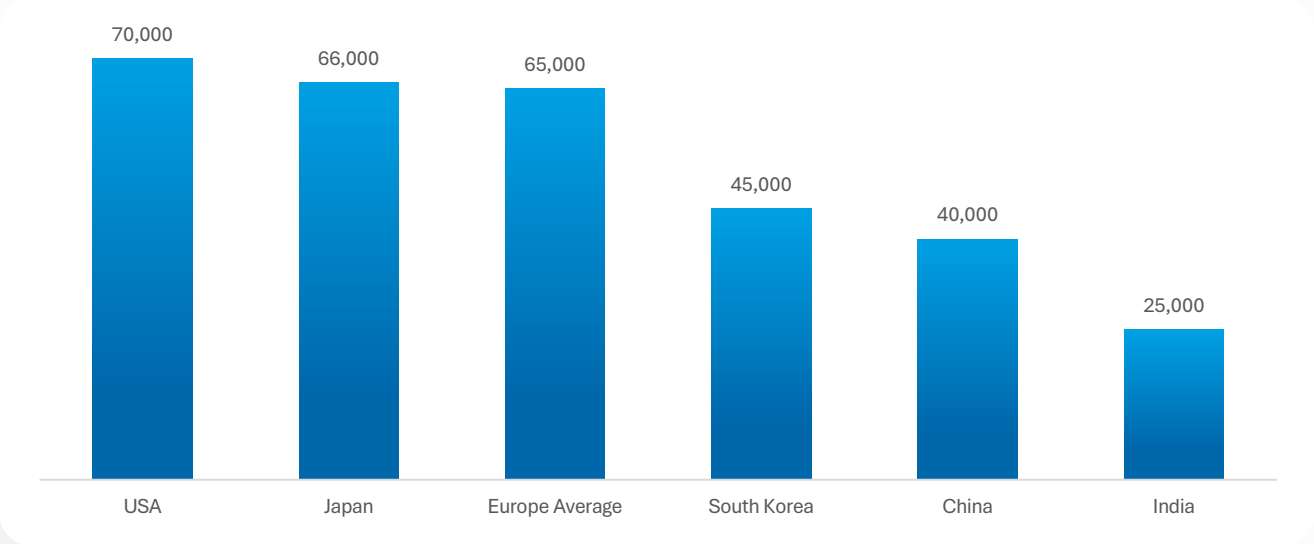
3. Access to fungible capacities of CRDMO players provides flexibility, scalability and risk mitigation

CRDMO companies can put up larger capacities which are fungible across different clients, products and services. They can aggregate production and research needs from several innovators and in the process, spread their own invested capital and operational costs over multiple projects and products.

Thus, they can improve their own utilization of invested assets (human, financial, physical) and take the risk of low utilization away from innovators, thereby creating a win-win situation for everyone. CRDMOs can quickly scale up or down a certain business, accommodate varying demands, at various stages, in response to outcomes and demand from innovators.

4. Access to low-cost but equally skilled manpower located in emerging economies
Non-developed market economies provide equally skilled and high-quality manpower at various stages of the R&D chain at a much lower cost compared to their home geographies.

Chart 10: Annual salary of an average mid level scientist in country (in US$)



Source: *ValueQuest Internal Research, Bloomberg*

5. Access to innovation and specialized knowledge and technology know-how
As CRDMOs work with multiple clients and do a lot of repetitive work, they have developed specialised expertise of their own on several areas relating to manufacturing and R&D. In the process, they have created innovative systems which are now being sold to clients for better efficiency and throughput.

In recent years, large CRDMO companies have become even more advanced than the innovators themselves in areas of advanced manufacturing technologies. Today, they own specialized and technically complex equipment and expertise in certain areas of drug development and manufacturing to produce stable drug formulations that are appropriately filled and packaged.

Hence, there has been a shift in the perception of CRDMOs from just a service provider to that of a development partner. Revenue models are also evolving from 'time and material' based to 'milestone and revenue/profit share' based.

CRDMOs now take on responsibility for development and production, invest in innovation and advanced technologies and bring their unique competencies, knowledge, and capabilities to the table.

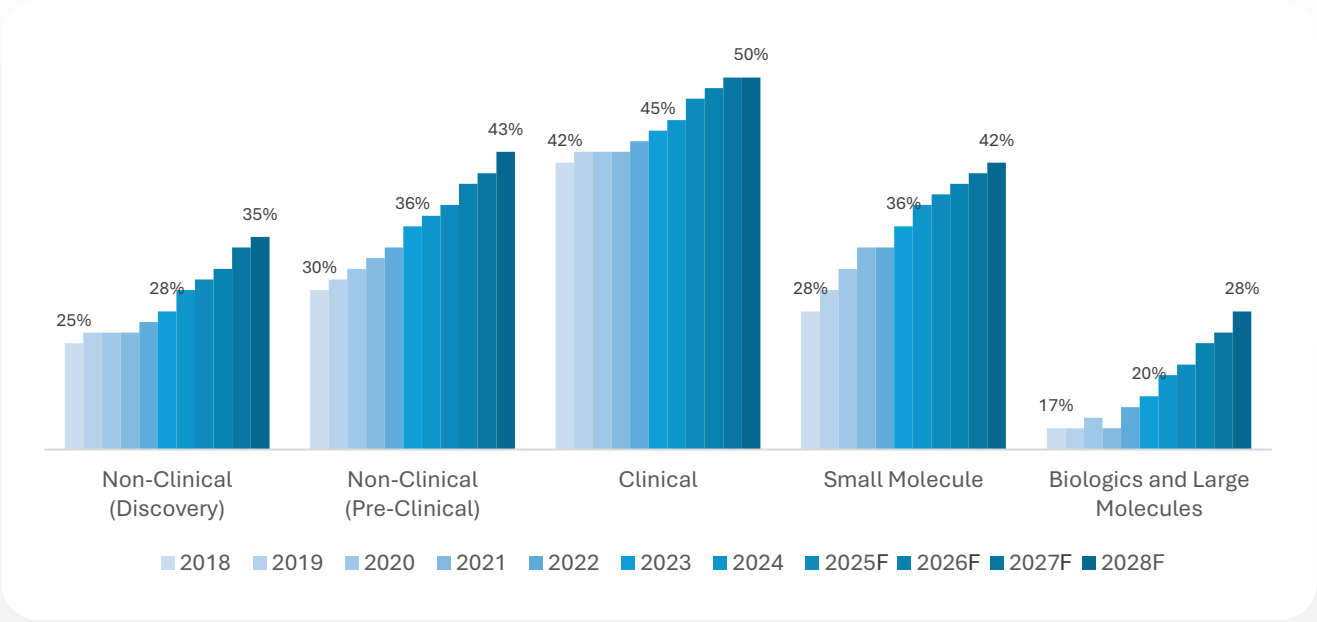
6. Reduced regulatory challenges

The pharma industry is subject to stringent regulatory oversight and compliance, which necessitates extensive expertise, resources, and various costs. Hence, outsourcing manufacturing to compliant CRDMO companies helps reduce regulatory costs and risks.

CRDMO Size and Growth Trends

As evident from the previous section, the trend of outsourcing has been increasing across all stages of the R&D value chain. Some stages such as clinical trials are easier to outsource and hence see higher outsourcing trends whereas others like discovery and biologics see relatively lower outsourcing due to concerns relating to intellectual property rights and secrecy.

Chart 11: Outsourcing trends across key areas in Pharma R&D (% of projects outsourced)



Source: *ValueQuest Internal Research, Frost and Sullivan*

Size and Growth of Industry

Because of the higher outsourcing trends across phases and across geographies, the CRDMO industry will continue to grow faster than the overall pharma market and R&D spends.

Chart 12: Pharma Market Shares and Historical and Expected CAGRs

		2018	2023	2028F	CAGR CY18-23	CAGR CY23-28F	CAGR CY18-28F
Global Pharma Sales	US$ bn	1136	1451	1956	5.0%	6.2%	5.6%
R&D Spend	US$ bn	214	277	325	**5.3%**	**3.2%**	4.3%
As % of Global Sales	%	19%	19%	17%			
Global CRDMO	US$ bn	127	197	302	**9.2%**	**8.9%**	9.0%
As % of Global Sales	%	11%	14%	15%			
Small Molecules	US$ bn	**85**	**113**	**159**	**5.9%**	**7.1%**	**6.5%**
As % of Global CRDMO	%	67%	57%	53%			
Biologics and Large Molecules	US$ bn	**41**	**83**	**143**	**15.1%**	**11.5%**	**13.3%**
As % of Global CRDMO	%	32%	42%	47%			

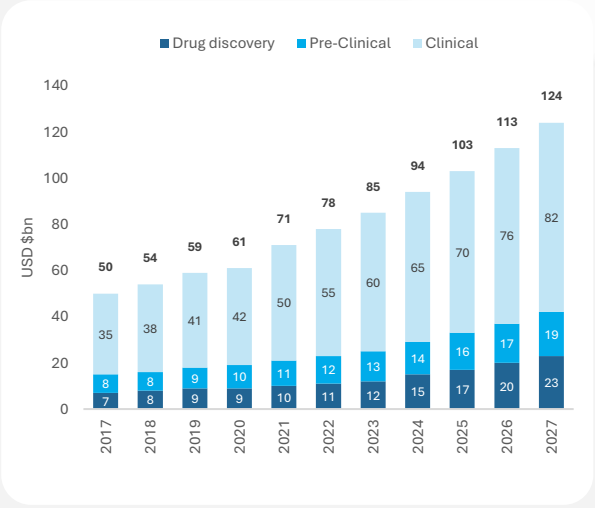
Source: *ValueQuest Internal Research, Frost and Sullivan*

Segmental Trends – Size and Growth Rates

Based on the nature of services provided and the absolute value of those services, CRO is smaller than CDMO as the latter involves actual manufacturing of API and formulations. Both are set to grow at healthy rates in the future, but, CDMO will continue to grow faster than CRO despite being on a higher base.

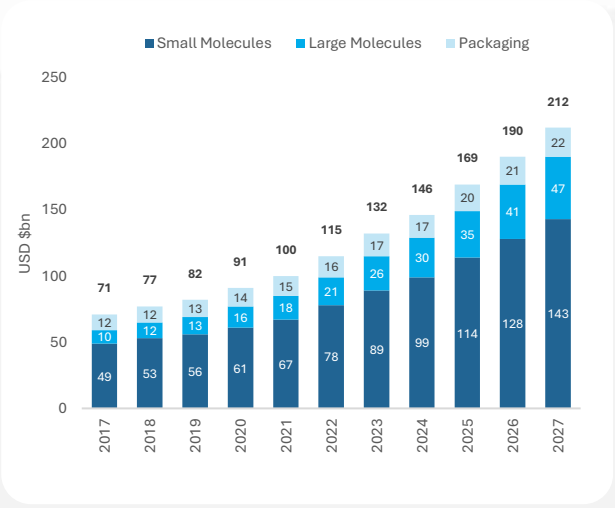
Drug discovery will grow faster within CRO while emerging modalities in Biologics will drive the growth in CDMO.

Chart 13: Global CRO TAM stood at ~US$78bn in 2022, with Clinical CRO the largest segment



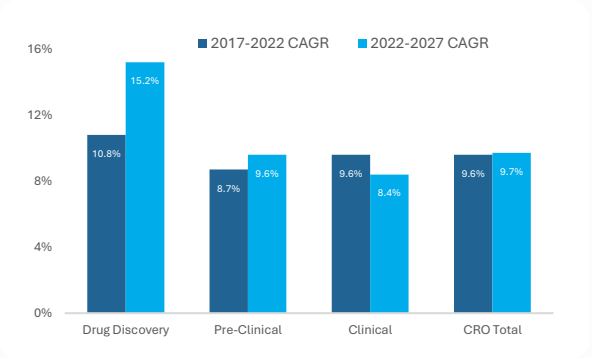
Source: *Frost and Sullivan, Compiled by Goldman Sachs Global Investment Research*

Chart 14: Global CDMO TAM stood at ~US$124bn, with small molecules dominating the majority state



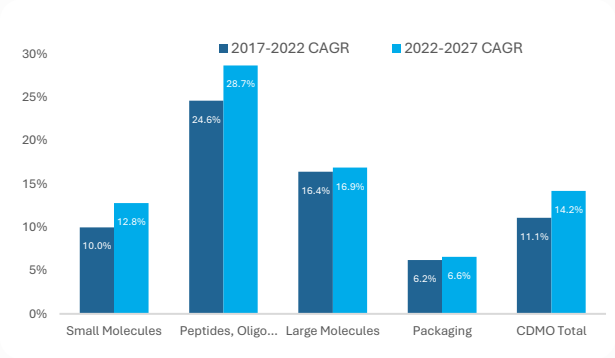
Source: *Statista, PWC Compiled by Goldman Sachs Global Investment Research*

Chart 15: Drug discovery is expected to be the fastest-growing CRO segment



Source: *Company data, Compiled by Goldman Sachs Global Investment Research*

Chart 16: In the CDMO market, peptides/ oligonucleotides/ CGT are expected to be the fastest-growing sub-segments followed by biologics



Source: *Company data, Compiled by Goldman Sachs Global Investment Research*

China's Rise in CRDMO
Has Shaped World Pharma

05

China's playbook for most industries has been to imitate advanced economies in terms of industrialisation and become better than them in terms of costs and quality over time through economies of scale and resultant efficiencies. However, in the case of Pharma, the Chinese government realised that it needed to incentivize innovation to truly move up the value chain. It named biotech as a strategic emerging industry in early 2010s.

Early 2000s

Generics Dominance and Regulatory Reforms

- Heavily reliant on generics
- Limited R&D capabilities.
- Introdued Good Manufacturing Practices (GMP)
- Aligned with global standards

2010–2015

Early Innovation and Policy Support

- Local companies began investing in biotechnology and biosimilars.
- Development of new drugs and biologics.
- Creation of national biotech parks and innovation hubs to boost research.

2016–2020

Acceleration of Innovation

- NMPA (Chinese FDA) accelerated approval processes
- Allowed clinical trials in China to run concurrently with global trials.
- More flexibility for drug developers.
- Increased spending on R&D by both domestic and MNCs
- Chinese companies like BeiGene and Junshi Biosciences launched novel treatments
- IPO Boom through Shanghai STAR Market and relaxed listing rules on HKSE

2021–2025

Global Expansion and First-in-Class Innovations

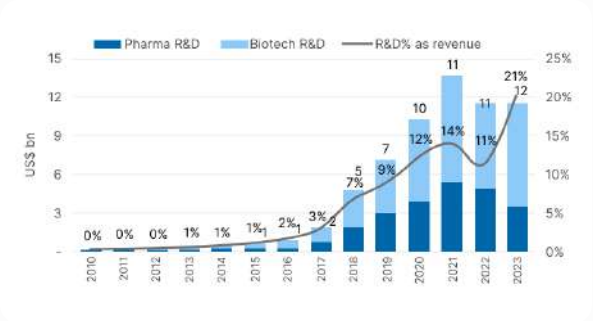
- First-in-Class (FIC) and Best-in-Class (BIC) Drugs with treatments for oncology, autoimmune and rare diseases.
- Global leader in clinical trial activity, government support and collaborations with MNC pharma
- Cross-Border Partnerships through out-licensing deals with global companies

Source: *ValueQuest Internal Research, WuXi Group, CLSA*

China's National Natural Science Foundation (NSFC), its largest public science funding organization and a major funding source for basic research and frontier exploration increased its research funding to encourage exploration and innovation, awarding 51,600 grants for a total of USD 4.5 billion in 2023. China's share of global biotechnology VC raised grew from a mere 3.5% in 2010 to 19% in 2023. Biotechnology VC raised by China – as determined by the VC financing raised by Chinese-headquartered firms – has surged.

Because of these initiatives, China's share in global pharma R&D has risen to significantly higher levels. Chinese New Active Substance (NAS) launches have increased significantly with 30+ launches for a 6th consecutive year, making the 5-year total 2nd after United States in global launches and surpassing European countries. Chinese institutions are also producing an increasing number of top-cited publications.

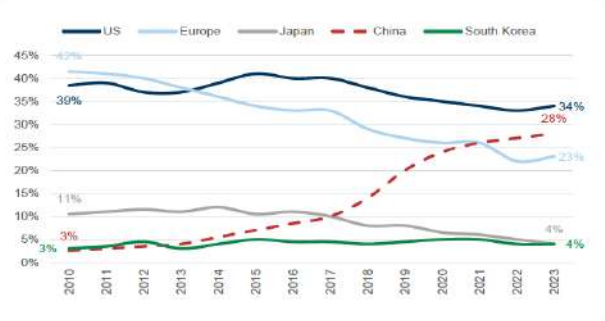
Chart 17: China domestic pharma + biotech R&D has seen exponential growth over the past decade...



Source: *Goldman Sachs*

Chart 18: ...leading to a sharp pick-up in clinical trial activity over the same period

Global share of Phase I and III starts based on company headquarters location

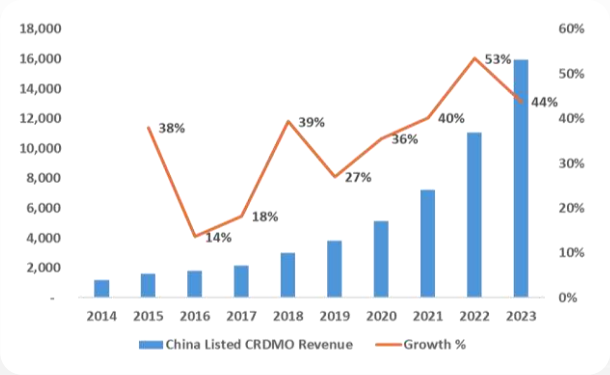


Source: *Goldman Sachs*

Chinese innovators entered into a number of out-licensing deals with EU and USA innovators and large pharma companies in the past 5 years.

Because of these initiatives, revenues and profits of Chinese CRDMO companies have also grown multi-fold over the past 10 years.

Chart 19: China listed CRDMO Revenue (US$ mn)



Source: *ValueQuest Internal Research, Bloomberg*

Chart 20: China listed CRDMO Earnings (US$ mn)

Source: *ValueQuest Internal Research, Bloomberg*

Case Study of WuXi Group

WuXi Apptec was founded by Dr Ge Li in 2008 as a CRO service provider. Over the next 15 years, it has evolved to become one of the largest CRDMO companies in the world.

Date	Acquisition	Focus/Business	Purpose	Headquarters & Operations
2008	AppTec Laboratory Services	Biologics manufacturing and services	Expanding U.S. footprint and biologics expertise	Philadelphia, USA; U.S. – based operations
2011	Medkey	Clinical Trials	Clinical trial and regulatory capabilities	China
2014	XenoBiotic Laboratories	Preclinical research services		
2015 – Delisted from NYSE				
Apr - 16	CRELUX Gmbh	Drug delivery and protein crystallography services	Supporting structure-based drug discovery efforts	Munich, Germany; Europe – focussed operations
Jul-17	STA Pharmaceutical	Small molecule development and manufacturing	Strengthening drug manufacturing capabilities with Couvet facility	Couvet, Switzerland; U.S., Europe and China
Jan-17	HD Biosciences	Preclinical drug discovery and biology services	Boosting preclinical discovery capabilities	Shanghai, China; Focus on Asia and global clients
Oct-17	ResearchPoint Global	Contract research organization (CRO)	Enhancing global clinical trial capabilities	Austin, Texas, USA; Worldwide CRO services
2018 – Relisted on SSE and HKSE				
May - 19	Pharmapace, Inc.	Biostatistics and clinical trial consulting	Expanding clinical trial services for pharma and biotech clients	San Diego, USA; U.S. and global clinical trials
Mar - 21	OXGENE	Gene therapy and CRISPR solutions	Strengthening capabilities in cell and gene therapy development	Oxford, UK; Global operations

Source: *ValueQuest Internal Research, WuXi Group*

WuXi AppTec initially founded WuXi Biologics as a biologics-focused division. In 2017, WuXi Biologics was spun off and went public on the Hong Kong Stock Exchange (HKSE) as an independent entity. Since the spin-off, it operates independently. However, both companies maintain complementary businesses and share the brand.

Year	Acquisition/Investment	Impact
2019	CMAB Biopharma	Increased biologics capacity and capabilities in China.
2020	Bayer's Wuppertal Plant (Germany)	Entry into European biologics manufacturing.
2020	Massachusetts (U.S.) site lease	Strengthened U.S. manufacturing footprint.
2021	Facilities in Singapore and Ireland	Global diversification of biologics manufacturing sites.

Source: *ValueQuest Internal Research, WuXi Group*

Over the years, the group has

- Built up capabilities across emerging technologies through organic and inorganic means
- Expanded in capacities globally, across key geographies like USA, Europe, Singapore, and China
- Built up a world class scientific talent base by recruiting Chinese and global expats from global innovator companies who have brought in business and helped improve the quality of their R&D efforts
- Ensured strong regulatory and compliance track record including IP protection
- Access to capital whenever needed by being listed on prominent global stock exchanges.
- Created its own fund to invest in emerging innovative companies in the biotech space globally.

Together, the WuXi group has a robust pipeline, with approximately 16% share in global clinical-stage drugs, a strong presence across all emerging modalities in small molecules and biologics, and end-to-end testing platforms. It caters to most leading global pharmaceutical companies in the USA and Europe. These initiatives have helped WuXi grow its asset base, revenue, profits, and cash flows multi-fold over CY2018–23, while maintaining a prudent net-cash balance sheet.

Thus, China has become critical to the global pharmaceutical ecosystem. A strong chemical supply chain, based on large integrated facilities, advanced research and development capabilities, cheaper and skilled labor, a large pool of scientific talent, lower operating costs (power, logistics) compared to developed markets, and strong government support and funding, have combined to make China the largest supplier of pharmaceutical chemicals and biologics to the world. The USA's imports of Chinese pharmaceutical and related products grew from USD 2.1 billion in 2020 to USD 10.3 billion in 2023 (a 485% increase). Chinese CRDMO companies are now involved in approximately 50% of drugs in clinical-stage development and around 33% in early-stage discovery and preclinical trials. Chinese CRDMO companies also support 66% of the drugs being developed by public companies in the USA, of which 60% have either been already marketed or are in late clinical stages.

WuXi group is the dominant player with its Biologics division being one of the largest manufacturing companies in the world, with numerous manufacturing partnerships. WuXi AppTec is among the largest research service providers globally and is widely used by cell and gene therapy (CGT) companies worldwide. Together, they manufacture 19 biosimilar and innovator drugs approved in the US, including several blockbuster drugs like Revlimid, Vertex's Trikafta/Kaftrio, BeiGene's Brukinsa, and Tirzepatide (the API in Eli Lilly's blockbuster weight-loss drug Zepbound). US companies accounted for 46% and 66% of WuXi Biologics' and WuXi AppTec's revenue, respectively, in 2023.

Source: *GlobalData's Pharma Intelligence Center Drugs by Manufacturer Database*

BioSecure Act To Reduce the China Dependency?

06

Prelude to the bill

Over the past 20 years, China has become critical to various industrial supply chains. Along with its economic rise, China also became militarily stronger and used its institutions to strengthen various facets of defence including biotechnology and pharma. Certain laws passed in the past decade have allowed the Chinese government to control and access data generated and used by Chinese companies including those in the pharma sector.

In general, under successive USA presidents starting from Mr. Donald Trump in 2016, China is increasingly being seen as a strategic threat to USA in various industries, leading to a rise in geopolitical tensions. As a result, the US government, through its agencies and government arms, has initiated a series of steps, such as the Unverified List (UVL) and the Inflation Reduction Act (IRA), to reduce dependence on China for various products and services. Companies falling on such lists face higher tariffs or a partial/complete ban on their products and services. Covid-19 led to a significant supply chain disruption in various areas and further drove the need to diversify away from China.

Bill gets introduced in US legislative branches

Certain Republican and Democratic members of the U.S. House of Representatives introduced the BioSecure bill on 25 January 2024. The bill alleged that five Chinese CRDMO companies (BGI, MGI, Complete Genomics, WuXi AppTec, and their subsidiaries and affiliates) were closely linked to the Chinese military and government arms in several ways, including financial transactions and academic collaborations. Further, it alleged that these companies collected private, confidential data, including genetic information of U.S. and other non-Chinese citizens, from U.S. pharma clients and shared it with the Chinese government, which, in turn, used it to advance its AI and biotech capabilities.

The bill aims to ban key Chinese companies involved in pharma R&D and hinder their emergence as strong global biotech players amid China's dubious national security laws. Indirectly, it seeks to incentivize pharma innovators to reduce dependence on China by diversifying their supply chains to other friendly geographies, avoiding the transfer of technology, and boosting local manufacturing. It prohibits U.S. federal agencies or companies that receive federal funds from contracting with or procuring services and equipment from "companies of concern" (defined as those headquartered in or subject to the jurisdiction of a foreign adversary's government and posing a threat to national security). Anyone collaborating with these companies is disqualified from receiving grants, loans, or contracts from executive agencies.

Once enacted, companies stated in the bill could face restrictions within 6 to 18 months after the bill's conversion into an Act.

In the last 11 months, the bill progressively passed through several committees with overwhelming majorities. However, it also underwent several amendments that diluted and delayed its passage, largely due to strong lobbying by the pharma industry and the impending presidential elections in November 2024. The bill was reviewed in the Senate (Upper Chamber) and had a chance to pass easily if it had been included in the National Defense Authorization Act (NDAA 2025), an annual defense bill. However, the bill was not included as part of the 93 newly filed amendments, leaving its passage in the previous Congress highly unlikely.

That said, considering that the U.S. government is now controlled by Republicans in both branches of the legislature (the House and the Senate), along with the executive branch under President Trump (a Republican with strong anti-China leanings), the chances of the bill being passed in 2025 have risen significantly in some form or another.

As it stands today, the bill softens the blow on pharma innovators reliant on China by allowing sufficient time—until 2032—to bring their exposure to the five Chinese companies down to zero. It also includes waivers and exceptions in cases of medical exigencies (e.g., a repeat of Covid). Since the likelihood of the bill passing remains slim, it will likely need to go through the normal legislative process again.

In any case, due to geopolitical tensions, the need to reduce reliance on China, and potential supply chain disruptions, innovators remain hesitant to rely solely on the Chinese CRDMO industry, even if the bill is shelved.

Response of the Pharma Ecosystem To the Bill

Chinese CRDMO companies reacted negatively to the bill. They have collectively opposed the bill and the allegations stated within it, viewing it as a geopolitical tool against China. Interestingly, most of them initially faced no major challenges to their business. WuXi Biologics reported strong H1CY24 results, adding 61 new projects (50% of which were from U.S. clients) compared to 46 in H1CY23. However, in recent months, new business has dried up for the WuXi group, and they are now in the market to sell manufacturing assets in the U.S. and Europe.

US Pharma innovator companies have acknowledged the low-cost good quality services of the Chinese CRDMO industry and pointed out that the bill will further push up the cost of drug development if they are forced to move their projects to European and US CRDMOs. But they also accept the fact that they are overly reliant on Chinese CRDMOs and would work to reduce dependency on the same.

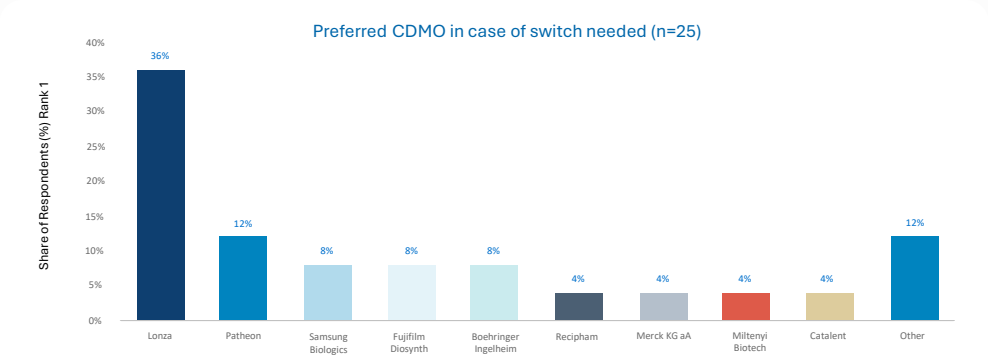
Rival CRDMO companies located in Japan, Europe, Korea, America, India, etc. expect no immediate benefits from this bill but do see increased inquiries and RFQs.

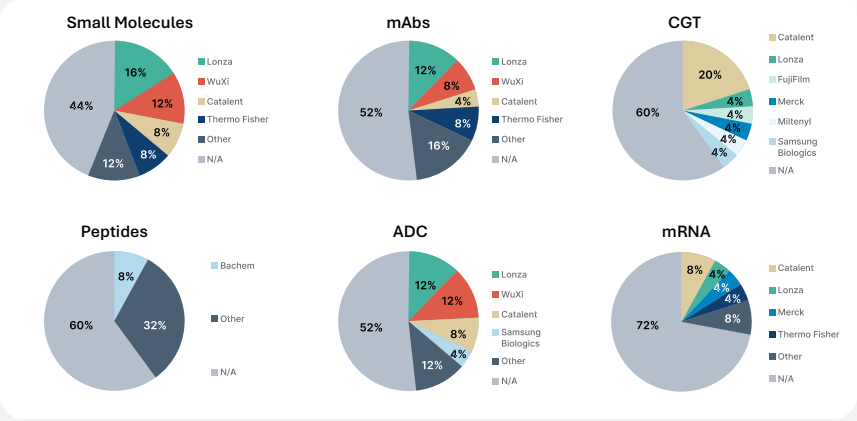
De-risking Dependency
Requires New Alternatives

07

The Biotechnology Innovation Organization (BIO) is one of the largest trade associations globally, representing biotechnology companies, state biology centers, related organizations, and academic institutions located in the U.S. and 30 other countries.

Surveys conducted by BIO and other prominent independent pharma research organizations, such as CPHI, as well as leading global sell-side financial research houses like Jefferies and Goldman Sachs, have all indicated that global innovators are willing to reduce their dependency on Chinese CRDMOs by switching to alternative large global CRDMO companies with capabilities in different areas. The majority believe that the time frame provided in the bill is sufficient for a smooth transition. Additionally, it would be easier and faster to move CRO work compared to CDMO work.





Source: *Jefferies*

Companies like Lonza AG, Samsung Biologics, and Fujifilm Diosynth have capacities and capabilities similar to those of WuXi. Hence, the initial benefit is most likely to accrue to them. However, over time, the benefits should percolate and spread to the wider CRDMO ecosystem based in lower-cost countries like India.

Learnings From
Global CRDMO Success Stories

08

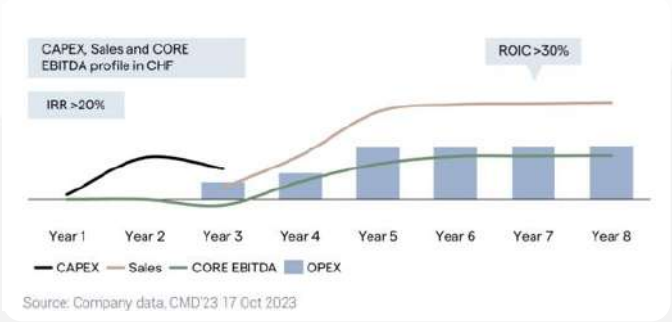
The industry has high entry barriers as innovators choose a partner not based on cost alone, but on several factors, including:

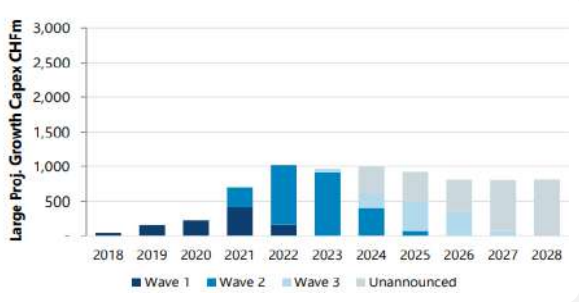
- **Compliance track record** – Regulatory, Environmental, Health & Safety (EHS).
- **Strong operational capabilities** – Scientific, technical, manufacturing, quality, innovation, AI, etc.
- **Reliability and consistency** – Strong delivery track record, consistent outcomes, and extensive experience.
- **Risk management** – Robust IP protection, data safety, integrity, and management.
- **Investments in capabilities** – Continuous and ahead-of-the-curve investments in capacities, infrastructure, and expertise.
- **Geographical diversity** – Flexibility to move operations from one site to another.
- **Integrated full-service operations** – Expertise across various stages of the value chain.
- **Competitive pricing** – Cost savings associated with building out technical and manufacturing capabilities.

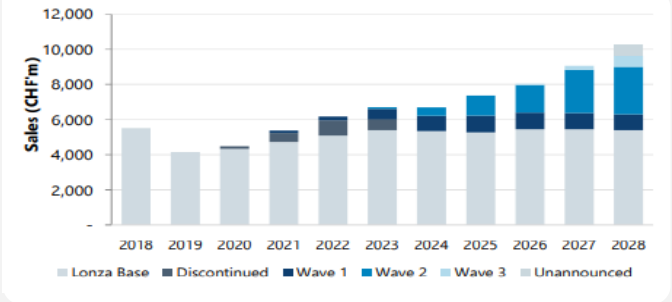
The CRDMO business is highly capital-intensive and long-gestation in nature. It requires significant upfront investments and capital expenditure (capex) in capacities and capabilities (scientific talent, research labs, manufacturing facilities, etc.) ahead of time to attract clients and secure potential business. Achieving an initial breakthrough to win a meaningful contract can take several years. Consequently, revenues follow with a lag of a few years. Invested assets can remain underutilized for extended periods if no sizeable contract materializes. Thus, the initial years often face negative profit margins and depressed ROICs (Return on Invested Capital).

Small project profile:

- Construction (Capex): 3 years;
- Faster ramp-up due to expansion of existing assets
- Peak sales in year 5;
- Peak Sales/ Capex ratio 1.05x
- Peak EBITDA Margin 43%;
- 15 year IRR: 18%;
- Year 7 ROIC: 27%;







Source: *Lonza, ValueQuest Internal Research*

There are several risks associated with such a significant initial investment, and navigating them is a challenge. Excess capacity comes with its associated unabsorbed costs, while insufficient capacity can lead to a loss of future business if a sudden surge in demand cannot be met by the vendor. Sourcing skilled and experienced talent is a perennial challenge, especially in developed markets. Additionally, regulatory compliance is becoming increasingly costly, even for CRDMOs. Maintaining financial discipline amidst these diverse challenges is a task in itself.

The switching cost for an innovator is high, as it must go through the entire regulatory process of validating a new partner. Consequently, savings of 10–15% usually do not justify a switch to a competitor.

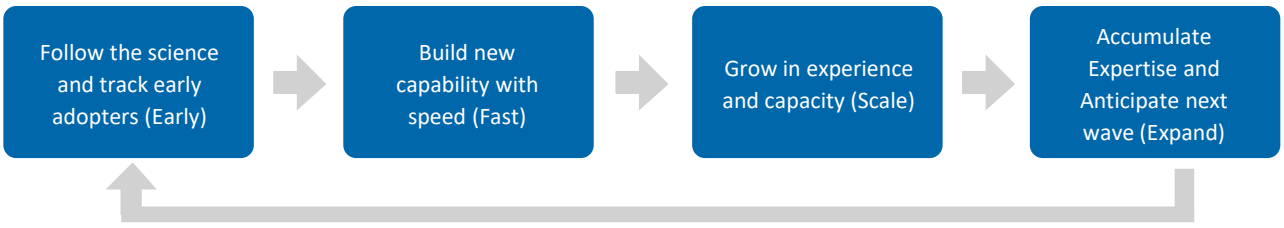
As a result, it is not easy for a new player to establish operations in this industry. The sector remains highly fragmented, consisting of thousands of small, limited-service providers, hundreds of medium-sized, moderately integrated providers, and a small number of fully integrated large CROs with global operations and deep capabilities.

According to Jefferies, only 1% of global CRDMO companies generate annual revenues exceeding USD 500 million, but these companies account for 31% of the CRDMO market by revenue.

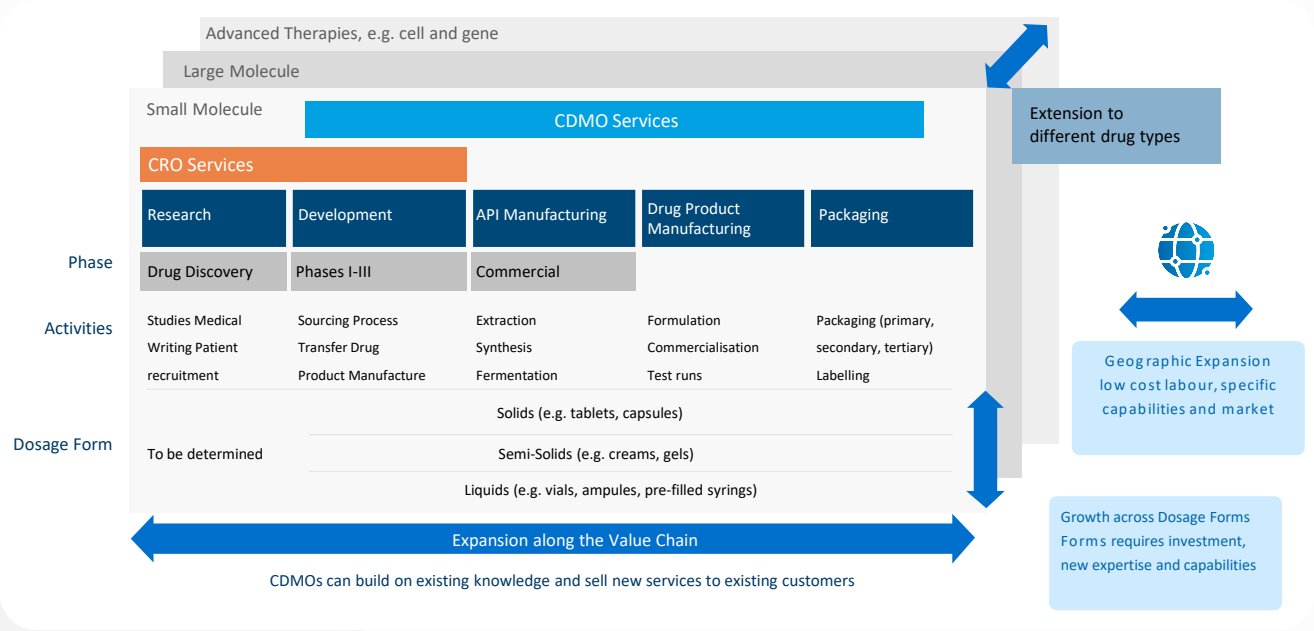
Source: *PharmSource Trends, Jefferies*

Areas of growth for the industry

Once a CRDMO establishes itself and navigates through the initial challenging years, it becomes a highly rewarding investment. The business tends to become sticky, with predictable long-term revenue streams characterized by steady and healthy operating margins and return ratios. It evolves into a self-sustaining virtuous cycle, where companies can leverage strong cash flows from existing operations to invest in new capabilities and expand capacities. Typically, large integrated CRDMOs have benefited from the flywheel effect of capability and business growth over time.



Thereafter, multiple avenues for growth become visible for a CRDMO company. Clients become more confident in its ability to provide services and often ask it to expand along multiple dimensions – more services in the same phase, entering other phases of R&D value chain, different drug types, different dosage forms, geographies, etc.



Source: *Piramal Pharma*

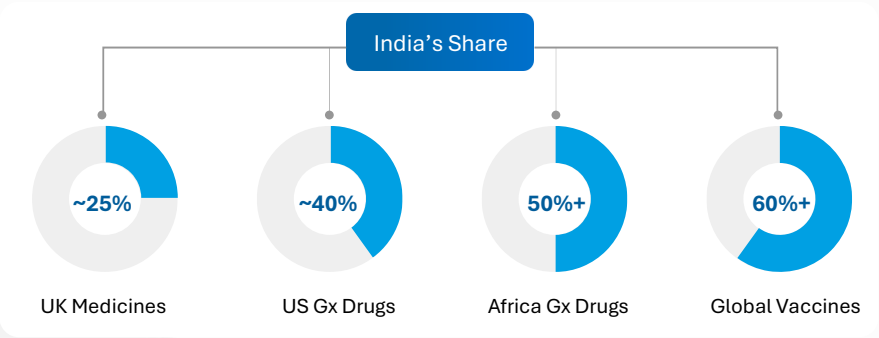
India's Opportunity To Lead in CRDMO

09

It is now evident that supply chain diversification efforts have gained momentum post-Covid-19, and the BioSecure Bill has further accelerated this trend. The focus is no longer solely on cost and efficiency but has shifted to resilience, reliability, and partnerships with companies based in countries that maintain friendly and favorable bilateral ties. Innovators are increasingly seeking alternate suppliers located in Europe, Southeast Asia (Korea), India, and other regions.

Large global beneficiaries such as Lonza, Samsung Biologics, and others are expected to benefit initially, as they possess advanced technological capabilities. Large molecule and biologics innovators prefer U.S., European, and Korean CDMOs (China+1) for their capacity and expertise. Meanwhile, small molecule innovators aim to diversify away from China while also reducing production costs (China+1, Europe/USA+1).

India is known as the Pharmacy of the World

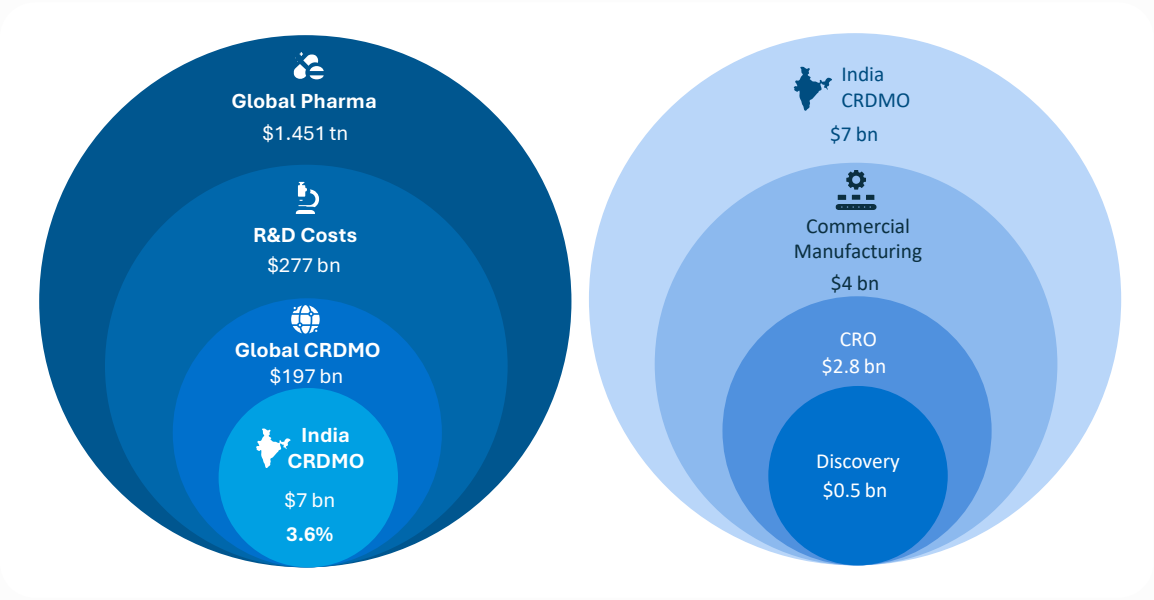


Source: *Avendus*

India supplies 25-60% of generic drugs and vaccines to the world. It has 3000+ drug companies and 10,500+ manufacturing units spread across key pharma hubs. India's unparalleled expertise in process chemistry has enabled the production of high-quality, reverse-engineered generic products at some of the lowest costs globally.

Indian CRDMO industry not a big player on world stage currently

However, when it comes to Pharma R&D, the Indian CRDMO industry's share is a minuscule 3.6% of the global CRDMO industry. The Indian CRO industry's market share stands at only 2.7% of the global CRO industry, compared to 16% for the Chinese CRO industry. The Indian CDMO industry's market share is even lower, at 1.6% of the global CDMO industry, compared to 8% for the Chinese CDMO industry.



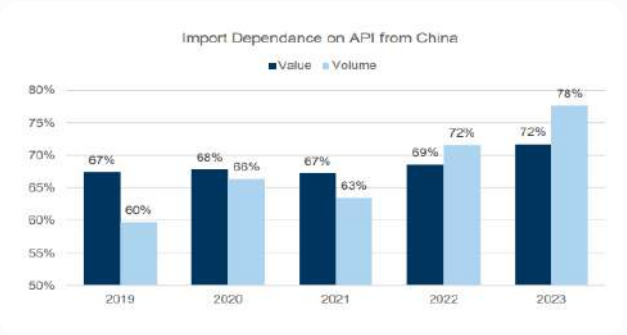
Source: *Frost and Sullivan (December 2023)*

The Indian CRDMO industry's capabilities and capacities have primarily been developed through bottom-up efforts and opportunistic plays by promoters and management teams of certain companies. Select Indian CRO and CDMO players have expanded their product offerings through both organic and inorganic routes.

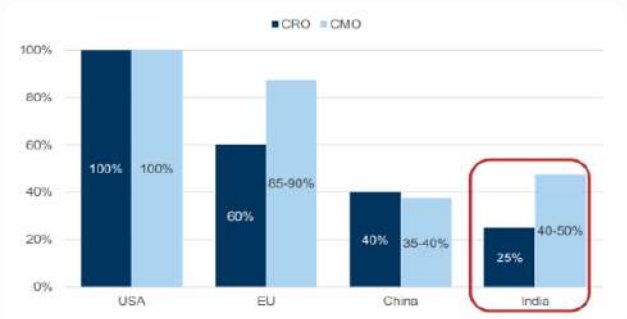
India remains dependent on China for sourcing Key Starting Materials (KSMs) and intermediates. Chinese CDMO companies operate at a much larger scale, giving them the advantage of negotiating higher discounts in exchange for larger offtake requirements. In many cases, KSMs are supplied by Chinese producers, further reducing lead times, logistics costs, and working capital needs across the supply chain. Additionally, government funding and incentives, such as tax breaks and large integrated common infrastructure facilities, lower operational costs for Chinese players in areas like environmental compliance and power.

As a result, the Indian CDMO and CMO industries are structurally disadvantaged compared to the Chinese CDMO industry, which operates at a significantly larger scale, valued at approximately USD 30 billion. Consequently, India's CDMO market share remains low, at just 2-3% of the global CDMO market. However, India is more competitive in the manpower-intensive, early-stage CRO industry, where dependence on China is minimal.

Chart 21: India's dependance on Chinese API has increased over the years



Source: Goldman Sachs



Source: Goldman Sachs

Indian CRDMO industry dominated by the small molecule CDMO industry

		2018	2023	2028F	CAGR CY18-23	CAGR CY23-28F	CAGR CY18-28F
Indian CRDMO	USD bn	4.0	7.0	14.0	11.8%	15.0%	13.4%
As % of Global CRDMO	%	3.1%	3.6%	4.7%			
Small molecules	USD bn	3.8	6.7	12.8	12%	13.8%	12.9%
As % of Total India CRDMO	%	95%	92%	91%			
As % of Global CRDMO - Small	%	4.5%	5.9%	8.1%			
Biologics and large molecules	USD bn	0.2	0.6	1.3	24.6%	16.7%	21.2%
As % of Total India CRDMO	%	5%	8.2%	9.2%			
As % of Global CRDMO - Large	%	0.5%	0.7%	0.9%			

Source: Frost and Sullivan

Global pharma companies had already begun diversification efforts due to supply chain disruptions originating from China. Environmental crackdowns in China between 2013 and 2017 prompted many smaller API/pharma companies to wind down operations. This led to a rise in API prices in China, forcing manufacturers to explore China+1 options for API sourcing. The COVID-19 pandemic further accelerated this trend. During the January-March 2020 period, China's API supplies were severely impacted by pandemic-related disruptions, creating opportunities for Indian API companies to step in and meet the demand. Additionally, widespread shortages of drugs and medicines led to stockpiling of both APIs and formulations, further benefiting Indian players.

The BioSecure Bill is expected to expedite the shift of API manufacturing away from China. Moreover, regulations like the Inflation Reduction Act are pressuring pharma companies to reduce the prices of both innovator and off-patent drugs. High operational costs in the USA, Europe, and Japan add to the challenges. Meanwhile, the increased focus of large Western and Chinese CRDMO companies is towards higher-value higher-margin Biologics outsourcing.

Hence, they will have no option but to look at Indian CDMO partners to meet their demands of small molecule API and FDF manufacturing outsourcing.

Thus, the Indian CRDMO market is largely dominated by CDMO (commercial manufacturing of both API and FDF). As of now, it is mainly led by generic (off-patent) molecules. The Indian CDMO industry enjoys a relatively higher share of ~ 6% of the global small molecule CDMO industry, because of its strong track record and developed capabilities in chemistry and process engineering of small molecules.

Indian CDMO industry is making efforts to improve its positioning in the Global Small Molecules CDMO Market

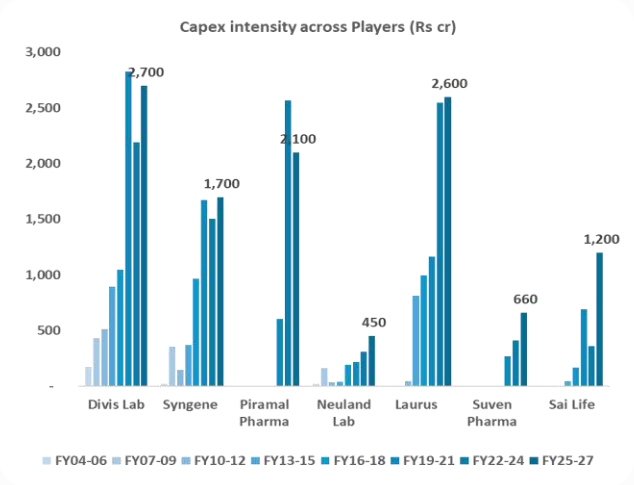
The high-value, high-margin and patented innovator focused API and FDF CDMO industry along with the high-margin CRO industry form a very small portion of the industry.
Historically, India has lacked the environment for a thriving high-value high-margin CRDMO industry due to a host of factors –

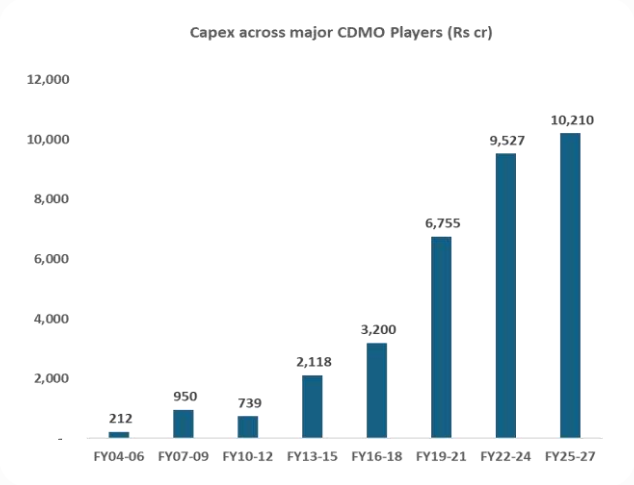
- Lower priority from a management strategy standpoint.
- Lack of sufficient funding, limited capital and lack of strong steady cash flows for the purpose of upfront investment
- Smaller scale of operations and capacities
- Limited collaboration between industry, academic institutions, and government
- Stringent and cumbersome clinical trial regulations in India
- Lack of incentives from the government to invest in R&D
- IP rights/patent system not strong enough for MNCs to invest in local R&D or collaborate with local companies

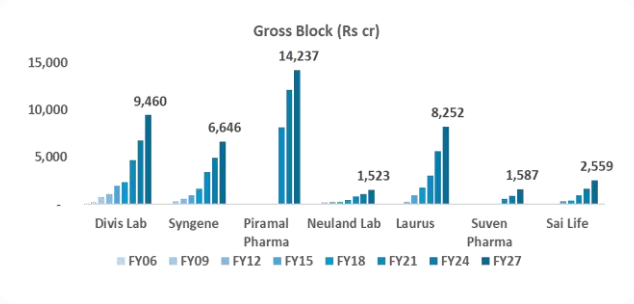
For India to establish itself as a significant player in the global CRDMO market, it must emulate China's approach in key areas such as scaling up capacities, enhancing quality and compliance standards, securing adequate funding, fostering government support, and driving extensive collaboration between academia and industry. India has made strides in many of these areas in recent years, signaling a positive trajectory for the industry's growth.

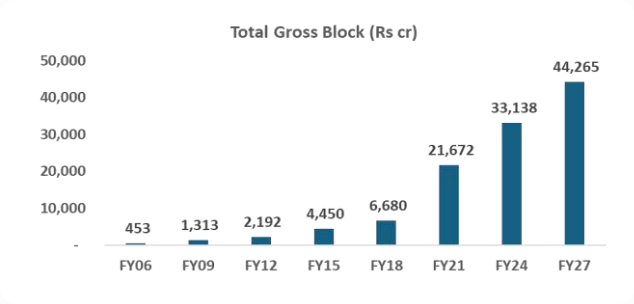
1. Large capex programs in recent years

Indian pharma companies are adding meaningful large capacities through large and sustained capex programs. The below charts showcase a group of 7 select pharma companies having CDMO operations undertaking increasingly larger capex programs over successive time periods.



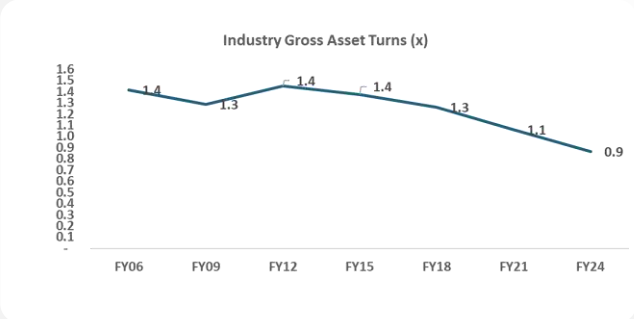


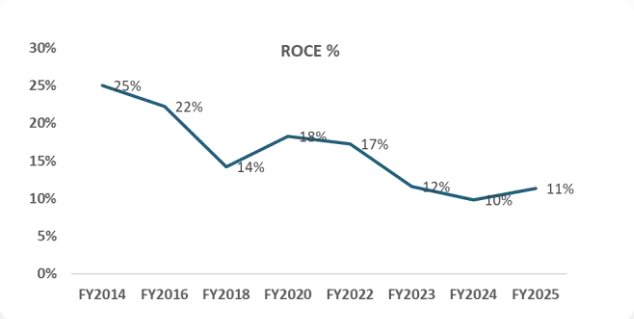




Source: *ValueQuest Internal Research, Bloomberg*

As we have seen previously, upfront capex drags asset turns and return ratios in initial periods. Industry's Gross Asset Turns and ROCE have declined during this time period.

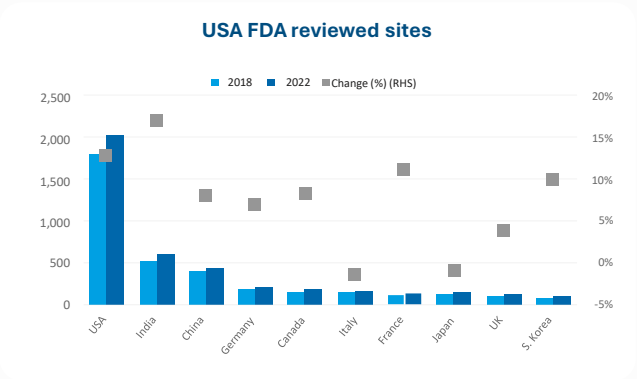


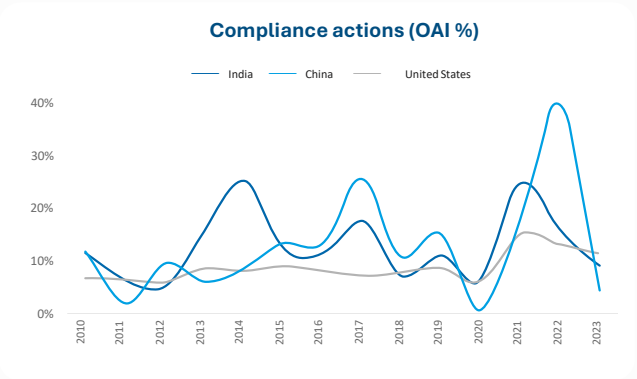


Source: *ValueQuest Internal Research, Bloomberg*

2. Large capex programs in recent years

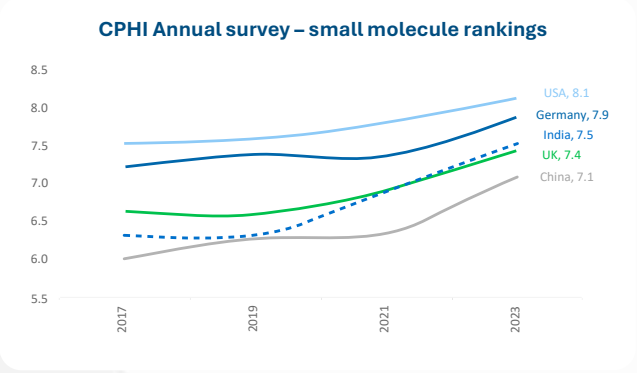
From a manufacturing standpoint, India has highest number of US FDA-approved facilities after US. Thus, Indian CRO/CDMOs are a natural choice of partner for Big Pharma for small molecules and synthetics. The Indian industry has improved its quality and compliance track record over the past few years which is reflected in the declining trend in adverse compliance outcomes in recent years.





Source: *Goldman Sachs*

A recent survey of global pharma professionals conducted by CPHI, a leading global event platform for the pharmaceutical industry, highlighted that India has improved its rankings in small molecule manufacturing, especially in FDF and knowledge of professionals.



CPHI Annual Survey	API	FDF	Overall competitiveness	Knowledge of professionals	Growth	Average
USA	7.6	9.0	7.4	9.1	7.5	8.1
Germany	7.8	8.9	6.7	9.1	6.9	7.9
India	6.7	7.6	7.3	7.9	7.8	7.5
UK	7.3	8.4	6.7	8.4	6.4	7.4
Switzerland	7.5	7.8	6.7	8.1	6.7	7.4
Japan	7.5	7.7	6.6	8.3	6.6	7.3
China	6.6	7.4	7.1	7.2	7.2	7.1
France	6.8	7.7	6.2	7.6	5.9	6.8
Italy	6.9	7.6	6.3	7.3	6.0	6.8
Singapore	6.3	7.2	6.3	7.6	6.5	6.8
Korea	6.8	6.7	6.7	6.1	6.5	6.6
Spain	6.9	6.5	6.5	6.1	6.7	6.5

Source: *CPHI (Convention on Pharmaceutical Ingredients)*

3. The Indian government is also playing its part by providing incentives and support in various forms

In last 10-15 years, India has gradually improved its ‘ease of doing business’ ranking by 4 to reach 10th among the 7 major economies of Asia in the 2023-27 forecast period. It is expediting regulatory processes to speed up approvals for new projects.

Through initiatives like Biotechnology Industry Research Assistance Council (BIRAC), Bio NEST, and Biotech Science Clusters, it is attracting local and global companies to set up R&D and manufacturing facilities in certain earmarked clusters for pharma companies.

It is incentivizing pharma manufacturing and giving tax incentives through Production Linked Incentive (PLI) scheme. PLI 1.0 aimed to reduce imports of critical Key Starting Materials (KSMs), Drug Intermediates (DIs) and APIs in India to spur local formulation and API manufacturing by giving Rs 20-400 Cr (depending on the product) for bulk drug park development. Financial incentives worth Rs 6900 Cr (USD 800 mn) were approved for manufacturers of 41 eligible products covering 53 APIs. PLI 2.0 was introduced to

enhance India's manufacturing capabilities by increasing investment, production and diversification to high-value goods. Many prominent Indian companies such as Aurobindo Pharma have participated in the scheme by investing in KSM facilities for products like Penicillin G.

Finally, under successive governments, India has also strengthened IP protection laws. Post the 1995 GATT accession and its 2005 compliance with TRIPS regulations, focus has shifted from process to product patents. MNC pharma companies are now less worried about patent infringement.

Thus, despite not being the cheapest on small molecule manufacturing, India will see more outsourcing of small molecule CDMO and should gain share in future.

India's CRDMO Industry		2018	2023	2028F	CAGR 2018-23	CAGR 2023-28F
Total CRDMO Industry	USD bn	4.0	7.0	14.1	12%	15.0%
As % of Global CRDMO	%	3.1%	3.6%	4.7%		
India Small Molecule CRDMO (includes both API and FDF)	USD bn	3.8	6.7	12.8	12%	13.8%
As % of Total India CRDMO	%	95%	92%	91%		
As % of Global CRDMO - Small	%	4.5%	5.9%	8.1%		
India Small Molecule Innovator API	USD bn	1.4	2.3	5.2	10.4%	17.7%
As % of Global Small Molecule Innovator API CDMO	%	5.1%	6.2%	10.1%		
As % of Global Small Molecule API CDMO	%	2.5%	3.2%	5.1%		
As % of Global Small Molecule CDMO	%	1.8%	2.3%	3.8%		
As % of Global CDMO Industry	%	1.6%	1.9%	3.0%		

Source: *Frost and Sullivan, ValueQuest Internal Research*

India is relatively weak in Biologics, but things are improving here as well

Spurred by pre-WTO era when India declined to agree to certain treaties, Indian law evolved to respect only process patents and not product patents. As a result, Indian pharma and chemical industry became good in chemistry R&D and manufacturing talent also evolved accordingly. Based on the limited capital and cash flows available with Indian promoters, their focus was entirely on scaling up their fledgling but attractive domestic and exports generic API and FDF manufacturing and marketing businesses.

Hence, they had limited capital and management bandwidth to focus their efforts on Biologics which was anyways a complex, long-gestation difficult-to-scale business. Their P&L and balance sheets didn't support the substantial upfront large investments needed in biological capabilities and capacities. Talent in the areas of biologics was also scarce.

As Indian pharma companies grew, they chose to move further up the value chain within small molecules such as HP APIs, complex generics, and specialty APIs. Some companies took the route of being the lowest cost producer globally in their molecules of strength by backward integrating into KSMs and intermediates.

However, things are changing here as well. The Indian CRDMO industry recognizes the high value high-margin growth potential of Biologics and has taken steps to be present in this area. Certain Indian CRDMOs like Piramal Pharma, Laurus, Syngene and select private companies have developed capabilities through organic and inorganic routes. Recently, Suven Pharma acquired NJ Bio, a US based company with expertise in this area. Laurus Labs invested substantial capital & brought in external investors for its Biologics wing, Laurus Bio.

Gradual market share gain in the high-value segment of discovery and pre clinical parts of CRO industry

1. India can gain share in Discovery CRO relatively easier and faster

Post the BioSecure bill, innovators are apprehensive of outsourcing the entire R&D process to Chinese firms, especially for early stage phases. Consequently, nearshoring has gathered pace as latter steps of the discovery stage are being completed in home countries. But USA and EU face a shortage of capacities and talent (which is only getting costlier). Thus, there is a need for a reliable alternate supplier in this part of the industry as well.

CRO is manpower intensive but not capital intensive. It requires a smaller set-up with certain special equipment for testing and laboratory work. Hence, CROs can be set up faster, take lesser time to scale up and have shorter timelines to start, if relevant manpower is available. CRO contracts are relatively shorter duration which allows innovators to switch relatively easily from one CRO to another.

India has always had a strong base of STEM graduates. Coupled with skills in chemistry and pharmaceuticals, these graduates are crucial for science-intensive drug discovery work. With a strong and growing supply of skilled manpower in areas of biology and chemistry, India is ideally placed to attract a larger pie of the CRO outsourcing. In addition, India already has an obvious cost arbitrage and is cost competitive against other major geographies including China. The cost of scientific talent in India is 60-70% cheaper than the cost in developed countries and 30-40% cheaper than the cost in China.

In recent years, many pure play R&D organizations or CROs have been set up in India by overseas Indian citizens and strong local talent. These firms have the intellectual vigour and niche capabilities, making them appealing to a broad clientele of innovators with very specific requirements relating to different stages of the process. Acquiring more customers is not going to be difficult once they prove their capabilities in execution and delivery.

As of now, a volatile and weak funding environment has slowed down CRO outsourcing growth. With improvement in funding, CRO outsourcing should improve. This improvement coupled with diversification and cost reduction initiatives, should benefit Indian companies in the coming years. This is reflected in the higher RFP/RFQ (Request For Proposals/Quotations) intensity in last few quarters for most Indian CRDMO companies.

2. India's track record in clinical trial services is weak, but it can improve with changes in regulations

India's large population provides the perfect diversity needed for any pharma drug clinical trial in terms of age, ethnicity, size, ailment, geography, climate, etc. Indeed, from 2000-2010, India saw a sharp rise in number of trials conducted by global pharma companies. However, many of them were conducted without following safety protocols and consent from trial participants. As a result, there were a series of high-profile mishaps including loss of human life. This led to a huge hue and cry, with the Supreme Court finally intervening in the matter and forcing the government to tighten regulations in 2013.

Guidelines made clinical trial agencies and the innovator companies liable for injuries caused to participants in the trials. Requisite regulatory permission to proceed with trials itself became very complex and was only given after a rigorous process. Hence, the approval process became lengthy and unpredictable. The overall cost of doing trials in India jumped 10-20x.

According to the Indian Society for Clinical Research, global clinical trial application approvals plunged from a high of 529 in 2010 to a low of 17 in 2013. Subsequently, India conducted only 70 global trials in 2014, 54 in 2015 and 44 in 2016. During 2013-19, less than 2% of global clinical trials took place in India. As a result, many research institutions and investigators discontinued clinical trials in India. Many Indian companies (such as Biocon, Piramal Enterprises, and Lupin) were also forced to go abroad to conduct clinical trials. Countries such as Malaysia, Singapore and Philippines emerged as major destinations.

Clinical trials form one of the largest segments by value, at around ~ 40-45% of the global CRDMO industry and have several 2nd and 3rd order benefits for the pharma ecosystem wherever executed. Hence, the Indian government crafted the New Drug and Clinical Trial (NDCT) rules in 2019, after studying best practices prevalent in USA, EU, and other prominent trial geographies. More comprehensive regulations were put in place to align with global norms, protect trial participants, improve data quality, and expedite the approval process. According to the senior management of a leading India-based CRO, the new rules have contributed to more trials coming back to India. Since 2019, global pharmaceutical companies have been optimistic on the regulatory support for conducting clinical trials in the country. This has resulted in the Indian clinical trial CRO market share improving slightly from 2.4% in CY18 to 2.8% in CY23. (Source: Frost and Sullivan)

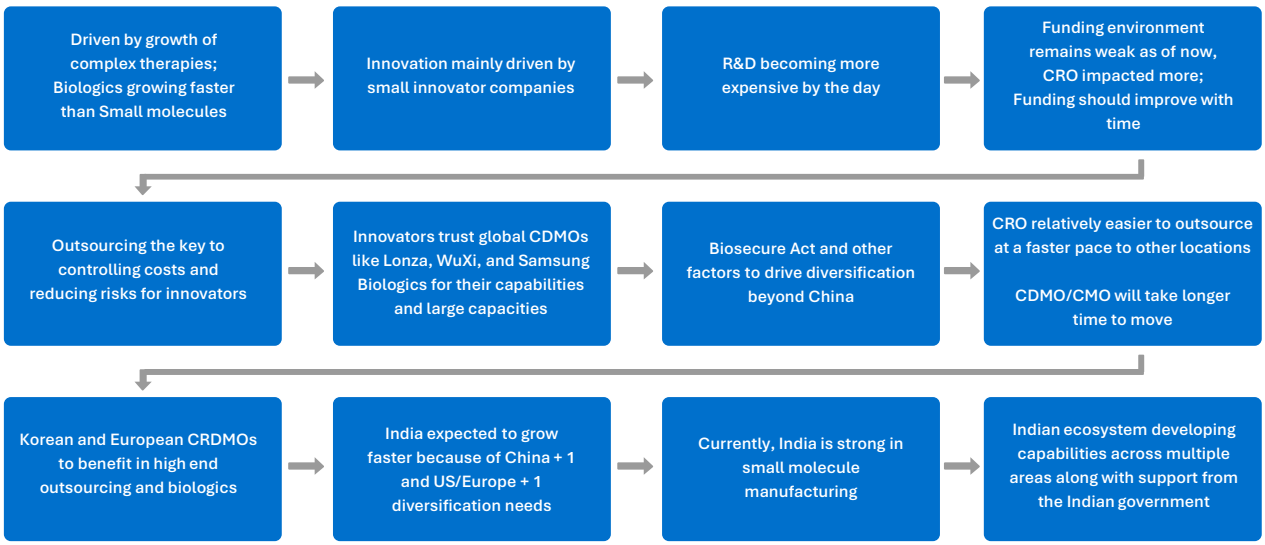
3. Thus, India is expected to see faster growth in outsourcing of discovery and clinical trials going forward

Outsourcing early-stage discovery and clinical projects is an important decision for many large and small pharma innovators and they take time to evaluate options. In many cases, they have given small exploratory projects to Indian CRO companies with a view to scale up relationships depending on delivery, execution, quality, and other factors. Conversion to the order book remains gradual for Indian CRDMO companies.

India's CRDMO Industry		2018	2023	2028F	CAGR 2018-23	CAGR 2023-28F
Total CRDMO Industry	USD bn	4.0	7.0	14.1	12%	15.0%
As % of Global CRDMO	%	3.1%	3.6%	4.7%		
Discovery	USD bn	0.3	0.5	0.8	11%	9.9%
As % of Total India CRDMO	%	8%	7%	6%		
As % of Global CRDMO - Discovery	%	3.3%	3.8%	4.0%		
Preclinical	USD bn	0.2	0.3	0.6	8%	14.9%
As % of Total India CRDMO	%	5%	4%	4%		
As % of Global CRDMO – Pre-Clinical	%	3.3%	3.0%	3.3%		
Clinical	USD bn	1.3	2.5	5.0	14%	14.9%
As % of Total India CRDMO	%	33%	36%	35%		
As % of Global CRDMO – Pre-Clinical	%	2.5%	2.8%	3.5%		

Conclusion 10

We summarise various facets of our extensive discussion in this simple-to-understand flowchart



The Indian CRDMO industry is set to grow at a much faster rate in the future compared to the past, driven by multiple growth drivers as explained in these sections.

Industry Size ($ bn)	2018	2023	2028F	CAGR 2018-23	CAGR 2023-28F
Global CRDMO Industry	127	197	302	9.2%	8.9%
North America	54	83	116	9.0%	6.9%
As % of Global	43%	42%	38%		
Europe	38	49	78	5.2%	9.7%
As % of Global	30%	25%	26%		
China	10	25	42	20.1%	10.9%
As % of Global	7.9%	12.7%	13.9%		
India	4	7	14	11.8%	14.9%
As % of Global	3%	4%	5%		
APAC (ex – India, China)	13	20	32	9.0%	9.9%
As % of Global	10%	10%	11%		
RoW	8	13	20	10.2%	9.0%
As % of Global	6%	7%	7%		

Source: *ValueQuest Internal Research, Frost and Sullivan*

However, it is not going to be widespread across segments as expected, but selective based on certain strengths and weaknesses of the Indian ecosystem. We highlight and debunk certain myths and narratives in the process.

Narrative	Reality
BioSecure Bill has already passed	BioSecure Act not yet enacted into law, already diluted
India will replace China soon	China is too big and difficult to replace easily or fast enough
Indian companies are innovative and can get business easily	India is behind in the innovation curve, has a lot to catch up to
India to benefit the most from diversification	**India has 'Right to Win' only in certain segments**
	Small molecule API manufacturing – both in innovation and generic APIs – driven by diversification requirements
	CRO – more on the discovery side – driven by conducive regulation, cost competitiveness & ease of switch

Risks

CRDMOs require substantial initial investments in the form of upfront capital expenditure in fixed assets and investments in a skilled workforce which are not easy to obtain. Winning business from innovator clients is a long-drawn process and takes several months to years. In the meantime, CRDMO companies have to make do with lower utilization of their operating assets leading to sub-optimal returns on investments for the first few years. This requires a fine balancing act between aggressive business acquisition practices and maintaining financial discipline (in areas such as profitability, working capital, capex, and funding the balance sheet via a judicious mix of debt and equity).

In addition, CRDMO companies need to comply with all the regulatory requirements of different countries in various areas relating to manufacturing, IP Protection, data integrity, environmental norms, health and safety, risk management, etc. Failure to do so can lead to significant negative impact on existing and future business.

While external tailwinds are in place, it is also upon Indian CRDMO companies to ensure that they deliver on the expectations of the clients in the form of consistent, reliable, and timely delivery of services and products at reasonable costs. Failure to achieve these multiple goals can affect future business.

Regulatory tailwinds form one of the cornerstones of a strong growth outlook for Indian CRDMO industry. If there is any dilution or cancellation of these tailwinds (such as not reducing sourcing from China), it can significantly impair the growth prospects of the Indian CRDMO industry.

Annexure 11

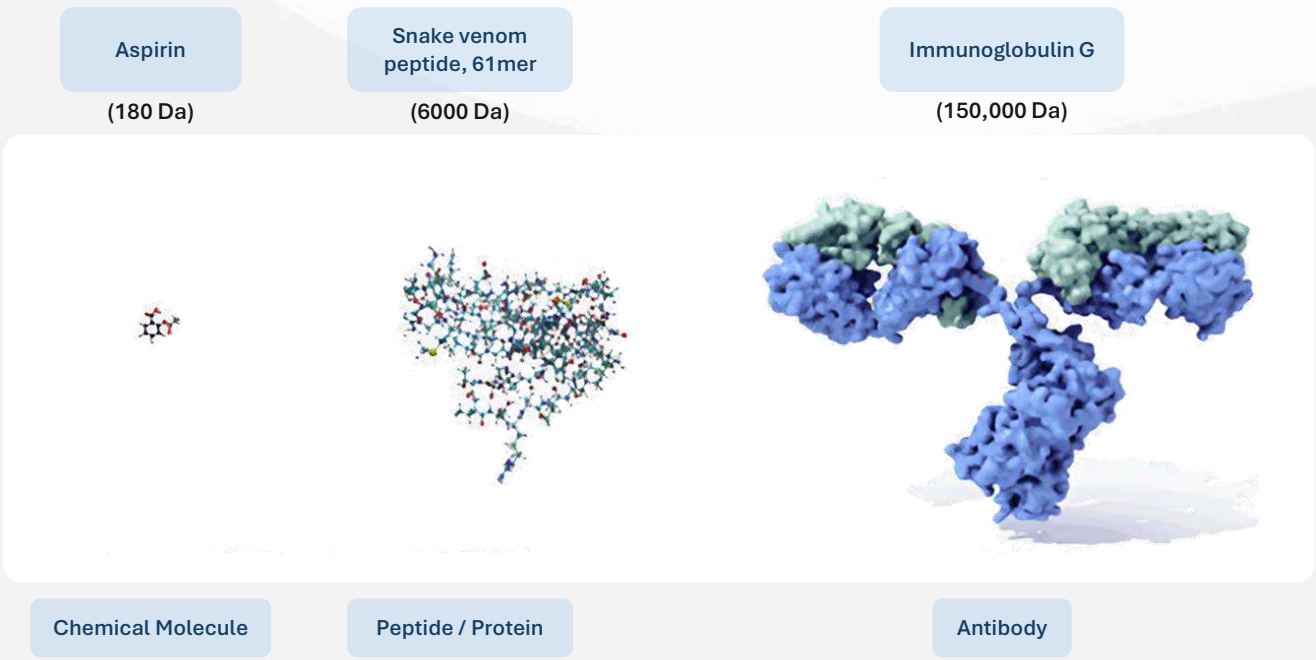
Pharmaceutical drugs primarily come in two forms:

Chemicals and **Biologics**.

Chemicals (Small molecules) have been around the longest and are low molecular weight compounds, typically less than 1 kDa (containing 20–100 atoms). They can be chemically synthesized through a relatively small number of steps and have high reproducibility. These include lipids, sugars, phenolic compounds, alkaloids & other classes of compounds.

Biologics, on the other hand, are classified as proteins that have a therapeutic effect. They have a high molecular weight, with more than 1,000 amino acids, typically ranging from a few kDa to 1,000 kDa. They are engineered to be identical to human proteins. These drugs are developed through **complex processes—synthesized, extracted, and purified** from live cells of living organisms—and **sometimes require more than 1,000 steps.** They often incorporate certain synthetic chemistry processes. Because of the intricate development process, they have low reproducibility. Biologics include vaccines, insulins, blood, blood components, gene therapy, tissues, and other protein-based treatments.

As seen in the picture below, based on their size and weight, chemicals are also called **'small molecules'** whereas biologics are also called **'large molecules'**.

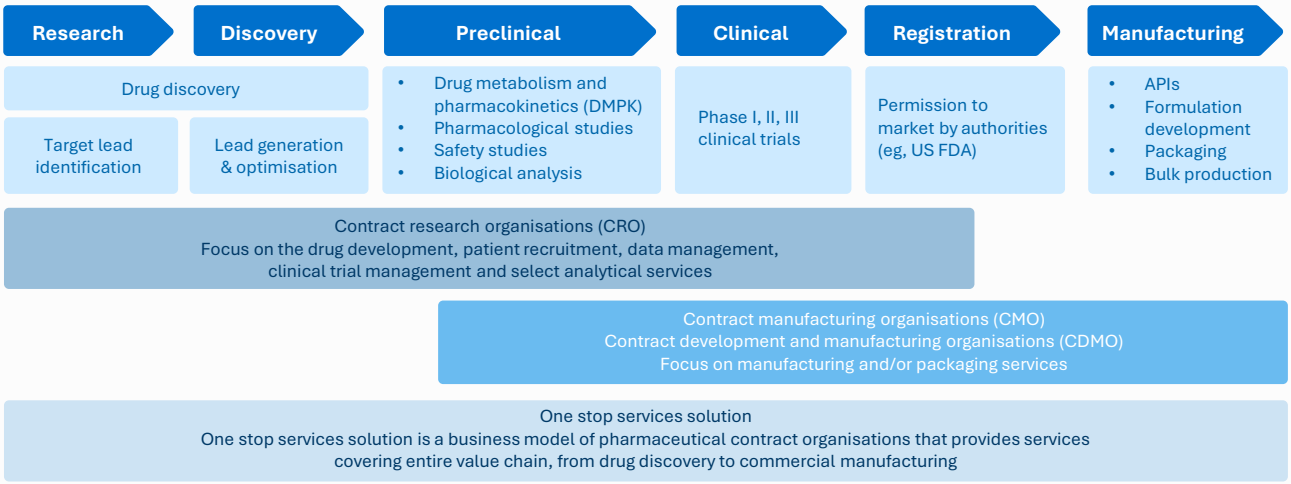


Small molecule drugs have been the mainstay of the pharmaceutical industry for over a century and known for their ease of manufacturing, cost effectiveness and affordability, ease of administration (largely oral), and broad therapeutic coverage. The current marketed portfolio of small molecules globally stands at 37000+ having a wide range of mechanisms to act against a broad array of ailments.

They account for ~65% of the total global pharmaceutical market by revenue in 2023.

In contrast, large molecule drugs are costly to manufacture and, at this time, in most cases, can only be administered by injection or infusion. However, because of their targeted actions, they are more amenable to treating some of the prominent unsolved ailments like cancer, neurology related ailments, and complex rare diseases which affect a smaller population but are of much higher value as an effective treatment can help prolong life or the quality of life itself.

CRDMOs take up some of the innovators' non-core work relating to the initial R&D stages, late-stage clinical trials and manufacturing activities.



CRDMO companies are mainly classified into 3 types:

1. Clinical Research Organisation (CRO) provide a wide range of services (scientific and non-scientific) in the discovery, preclinical and clinical stages of drug development. Those services include new drug discovery, R&D, clinical data management and NDA (New Drug Application) registration. Some CRO players focus on offering services at the preclinical and clinical stages. Preclinical services providers are mainly engaged in compound research and preclinical research support, including new drug discovery, synthesis and development of lead compounds and active drug intermediates, safety evaluation research services, pharmacokinetics, pharmacology and toxicology, and animal model construction. Clinical services cover phase I-IV clinical trial technical support, clinical data management, statistical analysis and assistance in NDA registration.

2. Chemistry Manufacturing and Control (CMC) / Contract Development and Manufacturing Organisation (CDMO) generally provide services relating to the drug substance (API which forms the core or active medicinal component of a drug) after it has been discovered. They normally come in at clinical stages to produce small batches of chemicals or biologics material ((both simple and complex) as required by innovators and are involved in multiple stages of synthesis. They may overlap with preclinical and clinical stages of CROs but are generally not involved in clinical trials which is generally done by CROs.

3. Contract Manufacturing Organisations (CMO) primarily cover the manufacturing aspect to support the preclinical, clinical and commercial stages of testing and developing the API compound. They are generally also involved in Drug Products services (formulations) which relate to fill-finish, containment, of API with other chemicals to give it a finished usable consumption form, sterilisation, temperature and environmental controls, packaging, serialization, labelling, shipments, etc.

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