CITELINE CLINICAL

White Paper

The Annual Clinical Trials Roundup

2024 Edition: Promising Road to Recovery

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Introduction: Total Trial Activities

Welcome to the 2024 edition of Clinical Trials Roundup. Last year, we unveiled a landscape of increasing complexity, culminating in an unprecedented decline of clinical trial initiations. The biopharma industry weathered post-pandemic adjustments, endured economic hardships and slowed growth in major markets, met regulatory pressures to incorporate diversity, equity, and inclusion (DE&I), and suffered the impacts of geopolitical conflicts. Last year, we concluded with a cautiously optimistic outlook, anticipating the industry's imminent breakthrough in clinical trial innovation.

Continuing with our annual tradition of Clinical Trials Roundup review, the 2024 analysis focuses on an overview of the Phase I–III clinical trials that initiated in the prior calendar year (2023) across all therapeutic areas (TAs) comprehensively covered by Trialtrove, as well as in-depth analyses into the key diseases, sponsoring companies, and geographies that impact the pharmaceutical industry. We will survey the recovery in clinical trial activity that occurred as the pandemic gradually de-escalated to an endemic and how it reflects the current clinical landscape.

As of June 21, 2024, Trialtrove curated 9,959 Phase I–III clinical trials (Table 1) investigating at least one drug and with a disclosed start date within the calendar year of 2023, returning growth of 9.4%, a remarkable recovery from the decline observed in 2022.[1] Looking at trial initiations since 2020, the pandemic-related fluctuations seem to have abated somewhat. The rise and fall of infectious disease (ID) trials reflected the industry's agility to adapt and manage the challenges brought by the pandemic. The 9.4% increase in 2023 is a notable achievement, surpassing the average total growth of 7.8% seen during 2017–23.

Over the last three editions of Clinical Trials Roundup, we have surveyed trial initiations with and without COVID trials to get a sense of how the pandemic impacted trial initiations in other TAs, namely the "COVID effect." The decline in 2020 (-4%) made sense, while 2021 enjoyed a surprising comeback at +22%. Then, trial initiations dipped back down to -6% in 2022, due in part to the harsh economic environment in biopharma. The yo-yo has swung back up in 2023, exhibiting 13% growth excluding COVID-19 trials, also a cut above the average growth rate of 7% for non-COVID trials during 2017–23. Will the oscillating cycles between growth and decline continue, or is the biopharma industry on track to full recovery?

1. The data snapshot dates for full-year activity are June 21, 2024; June 26, 2023; June 23, 2022; June 14, 2021; June 12, 2020; June 5, 2019; June 6, 2018; and July 6, 2017. Due to delays in reporting of trial activity, counts for prior years will have likely grown since the original data snapshot date.

Table 1: Phase I–III clinical trial activity by volume and growth, 2017–23

Year of trial initiation	2023	2022	2021	2020	2019	2018	2017
Trial count	9,959	9,104	10,410	9,819	7,765	7,606	6,794
Year-on-year growth (%)	9.4%	-12.5%	6%	26%	2%	12%	12%
Trial count (excluding COVID-19 trials)	9,654	8,541	9,077	7,424	7,765	7,606	6,794
Year-on-year growth (excluding COVID-19 trials, %)	13%	-6%	22%	-4%	2%	12%	12%

Source: Trialtrove, June 2024

Industry-sponsored trials, which accounted for over 70% of all trials initiated in 2023, have been a driving force in clinical research. Before analyzing the data to forecast the trajectory of clinical trials activity, let's evaluate their performance over the past five years, as presented in Table 2. The growth of industry-sponsored trials during pre-pandemic years (2017–19) somewhat mirrored that of the total trial growth in Table 1. That trend broke in 2020 due to the epic rise of non-industry-sponsored COVID trials (26% total trials vs. 5% industry trials). However, excluding COVID trial counts significantly narrowed that gap (-4% total trials vs. -8% industry trials). The huge gain of 22% from excluding COVID trials in 2021 was largely non-industry-sponsored, because only 6% were accounted for in industry-sponsored trials.

Table 2: Phase I–III industry-sponsored trials by volume and growth, 2017–23

Year of trial initiation	2023	2022	2021	2020*	2019*	2018*	2017*
Industry-sponsored trials	6,801	6,151	6,646	6,542	6,211	6,127	5,684
Year-on-year growth (%)	11%	-7%	2%	5%	1%	8%	12%
Industry-sponsored trials (excluding COVID-19 trials)	6,611	5,807	6,027	5,709	6,202	-	-
Year-on-year growth (excluding COVID-19 trials, %)	14%	-4%	6%	-8%	N/A	-	-

*Data accessed August 2023

Source: Trialtrove, June 2024

2022 had fewer trial starts across all fronts, but now we are starting to see industry-sponsored trials catching up as the number of COVID trials has diminished. 2023 certainly reflects a stronger comeback for industry-sponsored trials. While the "COVID effect" peters out over the last two years, clinical research in COVID-19 is here to stay as a mainstay within the ID TA. Going forward, we may have reached the point where we can scrap the "COVID effect" in future analyses.

Despite that optimistic note of a glowing return to trial starts in 2023, there remains a sense of restraint, as the overall increase of 9.4% still fell short of the 12% year-over-year growth in pre-pandemic years. Our annual edition of the Pharma R&D Review 2024 by Ian Lloyd cheerfully forecasted plenty of sunshine in the pipeline to hold off storm clouds on the horizon.[2] The trajectory of the clinical trials space is on the up as well, with sunshine just peering through the clouds. The cold reality of storm fronts tends to hit clinical trials before its impact trickles down to early-stage drug discovery, given the substantial cost of running the trials. Funding is still hard to come by, though there are creative avenues being explored through partnerships; navigating the regulatory guidance on DE&I in clinical planning hasn't gotten easier; companies will continue to face legislative pressures on pricing; and we are seeing lower success rates in clinical development compared to a decade ago.[3] Let us brave the rabbit hole and unravel what 2023 trial initiations can tell us.

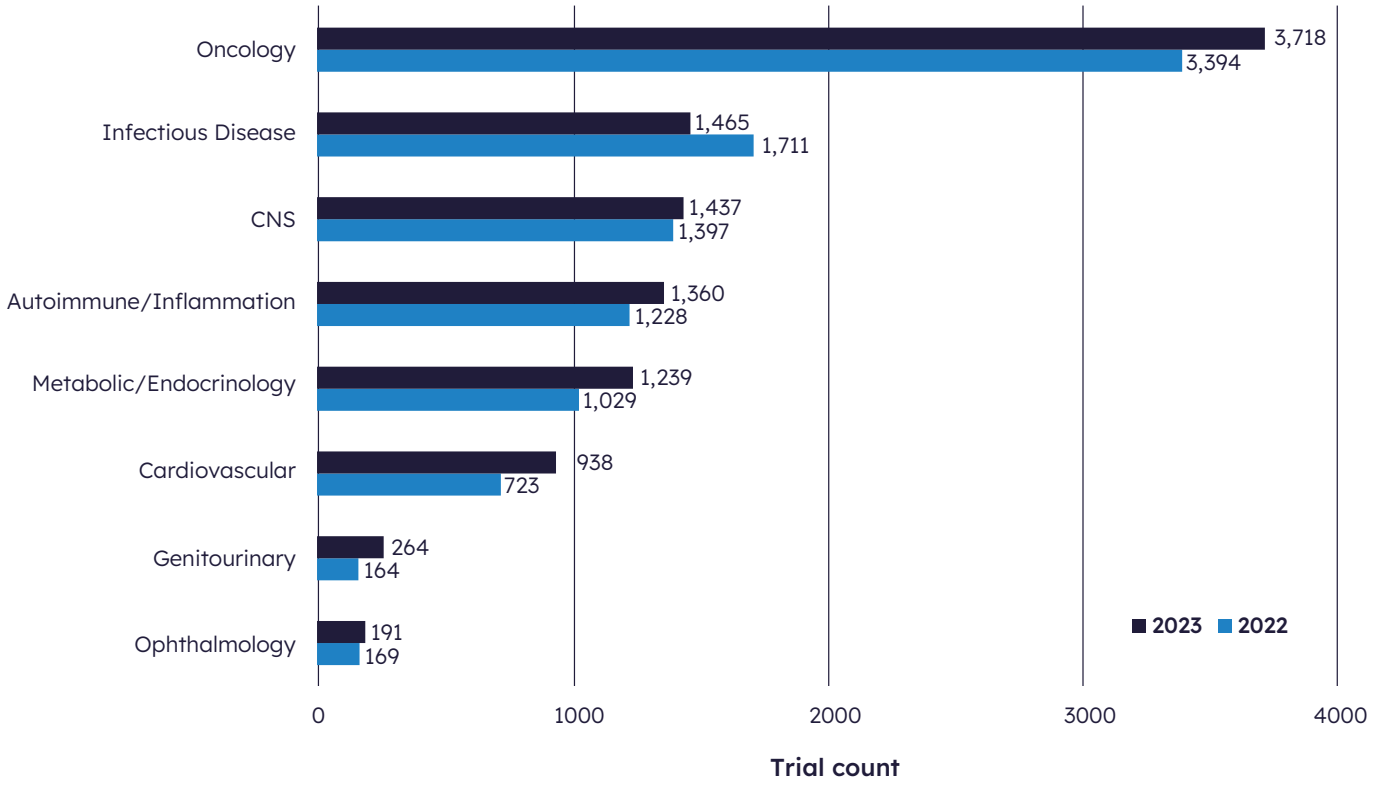
2. Citeline (2024) Pharma R&D Review 2024
3. Citeline (2024) Why Are Clinical Development Success Rates Falling?

Clinical Trial Activity by Therapeutic Area

The lineup of TAs by trial initiations has remained relatively unchanged since 2020, when the COVID-19 pandemic boosted the ID TA to second place, and it remains at this ranking to this day. Oncology continues to have a distant lead over all other TAs, as cancer remains the most prolific area of research. ID trials continue to recede as they have since 2021, narrowing the ID TA's lead over CNS. With the renewed boom in neurology and recent success in obesity drugs, it may soon be a toss-up between CNS and metabolic/endocrinology (MET) to snatch away the second position from the ID TA. Although CNS currently holds third place, it only posted 3% growth from 2022, while MET achieved more impressive growth of 20%. The cardiovascular (CVS) TA also experienced an uptick of 30% in 2023. Both the autoimmune/inflammation (A/I) and oncology TAs achieved similar climbs at 11% and 10% growth, respectively.

Ophthalmology (OPH) and genitourinary (GU) remained the two smallest TAs in the mix, switching places from 2022. It is worth noting that the number of GU trials went up by 100 in 2023, raking in 61% growth, the largest expansion rate of all TAs.

Figure 1: Phase I–III clinical trial initiations by therapeutic area[4], 2022–23



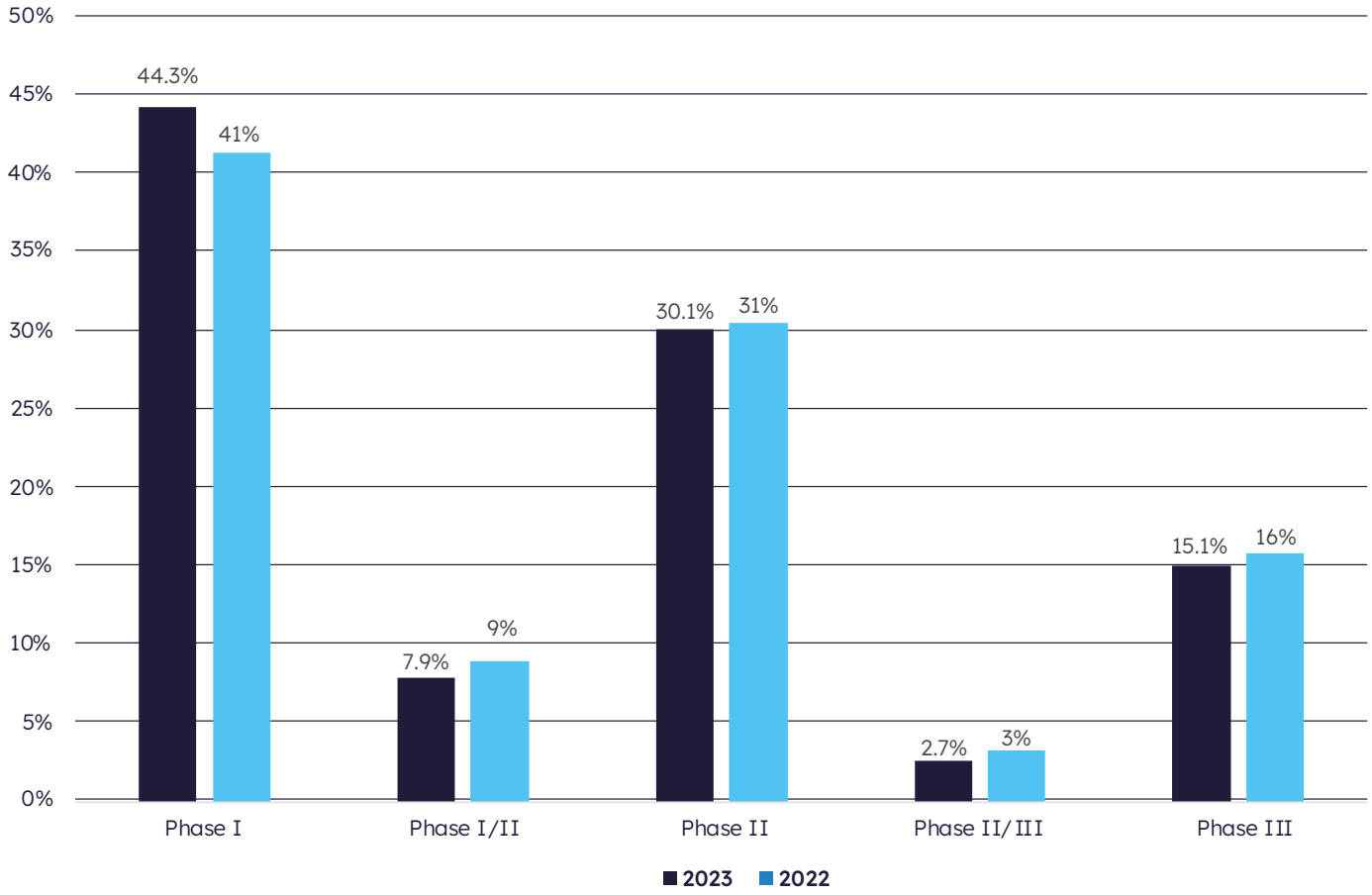
Source: Trialtrove, June 2024

4. Trials that include multiple indications across different TAs will be counted for each targeted TA. As such, the sum of trial counts for the eight TAs will be higher than the total number of Phase I–III trials started in 2023. Trial counts for ID include activity from vaccines (infectious diseases), which is a separate TA module within Trialtrove. For the purposes of this analysis, all ID activity has been combined into a single TA.

Phases of Trial Activities

A healthy clinical pipeline is typically characterized by a balanced distribution of drugs across the phases, with higher activity in the earlier phases and gradually shrinking as the compounds advance through attrition. That is exactly what we see over the last two years, though we see a slightly higher number of Phase I trials in 2023. Figure 2A offers a normalized view of phase distributions, showing the percentage of each phase against total trials in their respective years. The proportion of Phase II and Phase III trials appeared to experience little change, whereas Phase I trials grew by 3.3%, a sign of sustained innovation in the clinical pipeline.

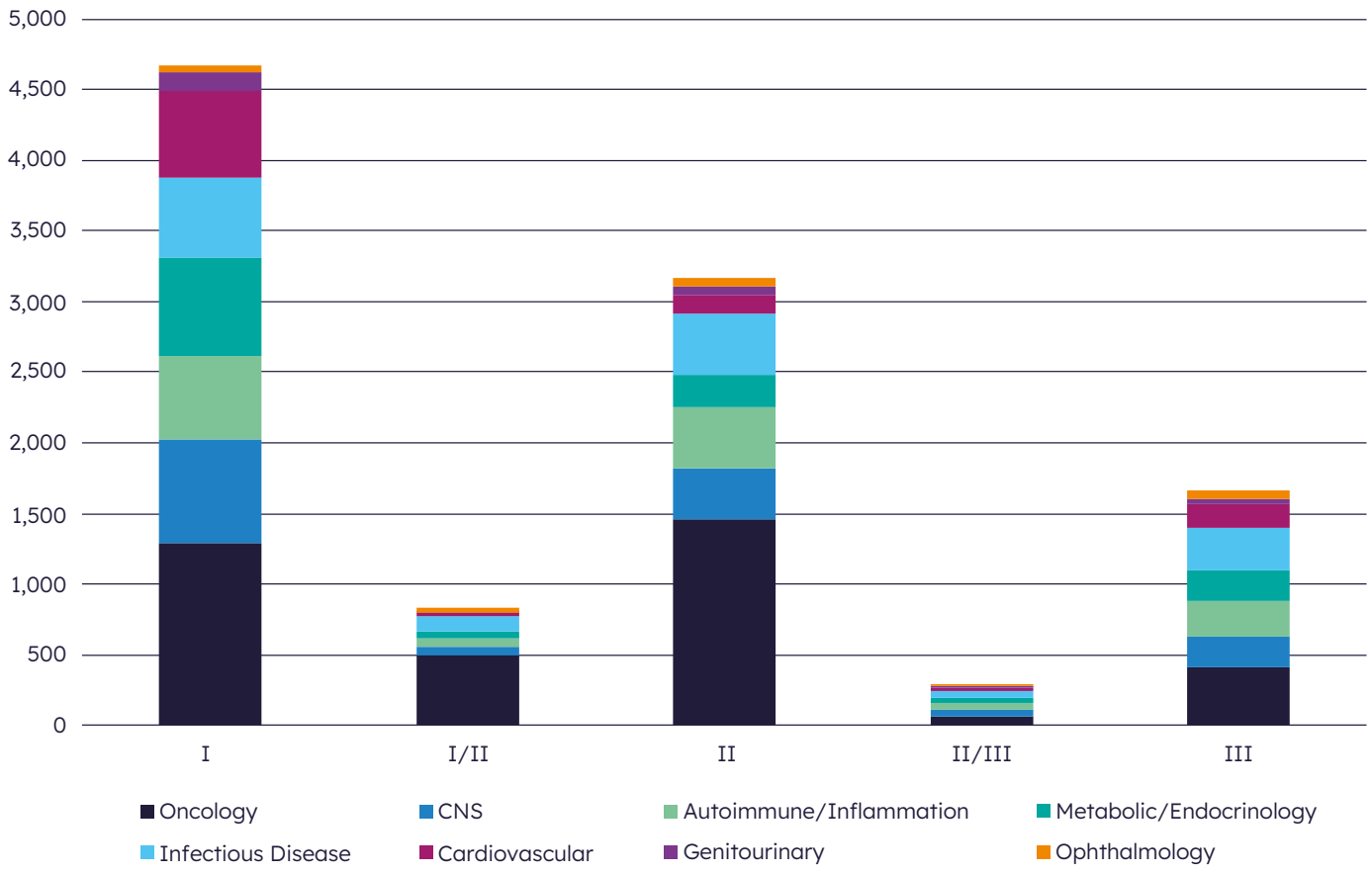
Figure 2A: Distribution of Phase I–III clinical trials by trial phase, 2022–23



Source: Trialtrove, June 2024

A closer look at the TA compositions by phase in Figure 2B reveals that the domineering presence of oncology in early phases shrank in Phase III, reflecting the persistent challenge in this TA to survive beyond Phase II clinical development. The CVS, CNS, and A/I TAs saw at least twice as many Phase I studies as Phase II studies, suggesting earlier attrition than oncology. Early discontinuations are suggestive of the R&D strategy whereby companies make go/no-go decisions earlier, thus cutting their losses of running more and larger trials.

Figure 2B: 2023 trials by phase and TA



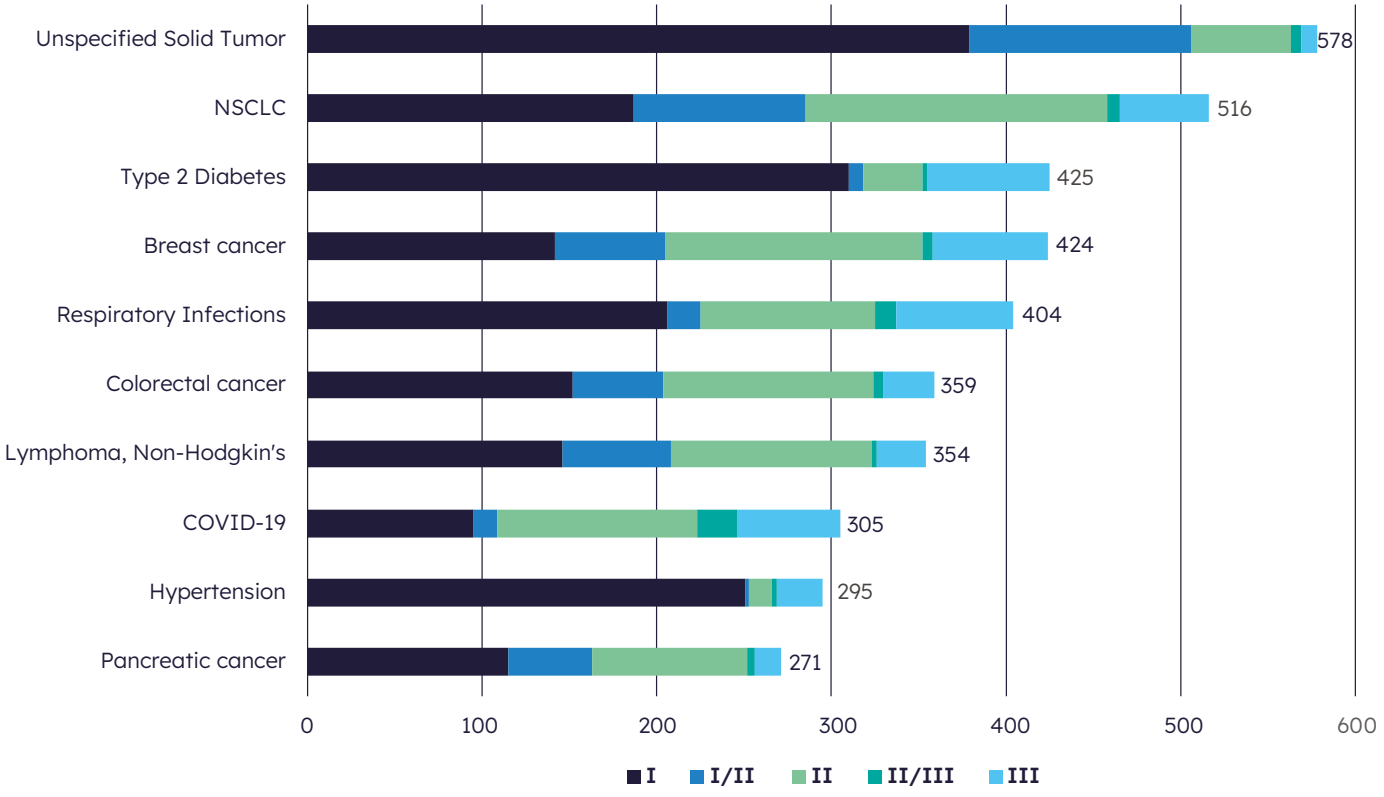
Source: Trialtrove, June 2024

Top Disease Areas of 2023 Trial Initiations

Each year we survey the top contenders of the most active diseases in clinical trials. The No. 1 spot in Figure 3 was finally reclaimed by unspecified solid tumor in 2022, and it retained its rank in 2023. The biggest upset is non-small cell lung cancer (NSCLC) ascending to second place, helping push COVID-19 down the rank from second to eighth place (Table 3). Oncology diseases comprised six of the top 10 list in 2023. Type 2 diabetes (T2D) had an impressive ascent from sixth to third place this year. The established success of Ozempic, Trulicity, and Farxiga brought fresh focus to this disease area, with additional promising contenders Mounjaro and Rybelsus emerging with impressive performances in 2023. Both respiratory infections and colorectal cancer moved up two positions, but non-Hodgkin's lymphoma (NHL) fell by two. This year, we welcomed new joiners hypertension and pancreatic cancer to round out the top 10, displacing respiratory vaccines and nociceptive pain from last year.

Given the large oncology presence in the top 10 diseases, most of its clinical development is early-phase heavy (Phase I–II). Unspecified solid tumor, NSCLC, breast cancer, and colorectal cancer are the hotbeds of trial initiations. T2D also had significant trial initiations in Phase I. As we turn our eye to Phase III trials, TA diversity becomes more prominent, given the top diseases here consisted of T2D, breast cancer, and respiratory infections.

Figure 3: Top 10 diseases in Phase I–III clinical trial initiations, 2023



Source: Trialtrove, June 2024

The steady upward trend of rare disease R&D also suffered a setback in 2022, with 13% fewer trial initiations than the previous year, wiping away the post-pandemic rebound observed in 2021 (Figure 4).

Table 3: Top 10 diseases and their ranking comparisons to 2022

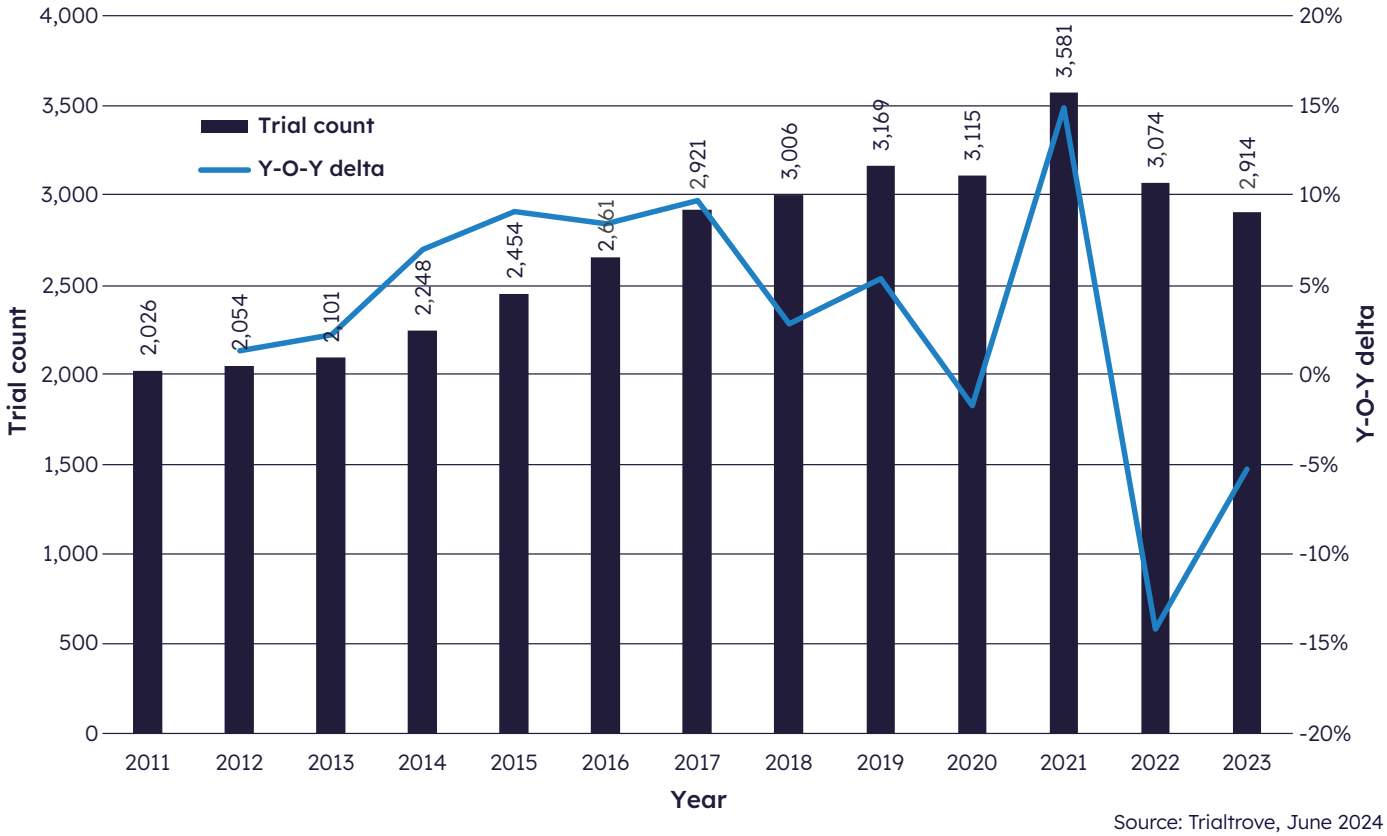
Diseases	# of trials	Rank (2022 rank)
Unspecified Solid Tumor	578	1 (1)
NSCLC	516	2 (3)
Type 2 Diabetes	425	3 (6)
Breast cancer	424	4 (4)
Respiratory Infections	404	5 (7)
Colorectal cancer	359	6 (8)
Lymphoma, Non-Hodgkin's	354	7 (5)
COVID-19	305	8 (2)
Hypertension	295	9 (12)
Pancreatic cancer	271	10 (15)

Source: Trialtrove, June 2024

A Word About Rare Disease Trials

Speaking of the top diseases, we must not overlook the important progress achieved in the rare disease areas. Citeline defines a rare disease as one with a prevalence of below 1 in 2,000 people in the EU or affecting fewer than 200,000 people in the US (equivalent to around 1 in 1,600 people). The steady climb over the last decade in Figure 4 peaked in 2021 with 3,581 trials but dipped back down to pre-pandemic levels in 2022 and 2023. As clinical trials become more complex and expensive over the years, this is even more the case for rare diseases, as these inherently niche areas face harder circumstances with patient enrollment, retention, and follow-up. The steep setback of rare disease trials in 2022 (-14%) wiped away the rebound gain in 2021; however, the decline in 2023 was less severe at -5% with 2,914 trials. Rare disease trials represented 29.3% of the total 2023 trial initiations, which is consistent with its proportion in prior years, ranging between 27% and 30%.

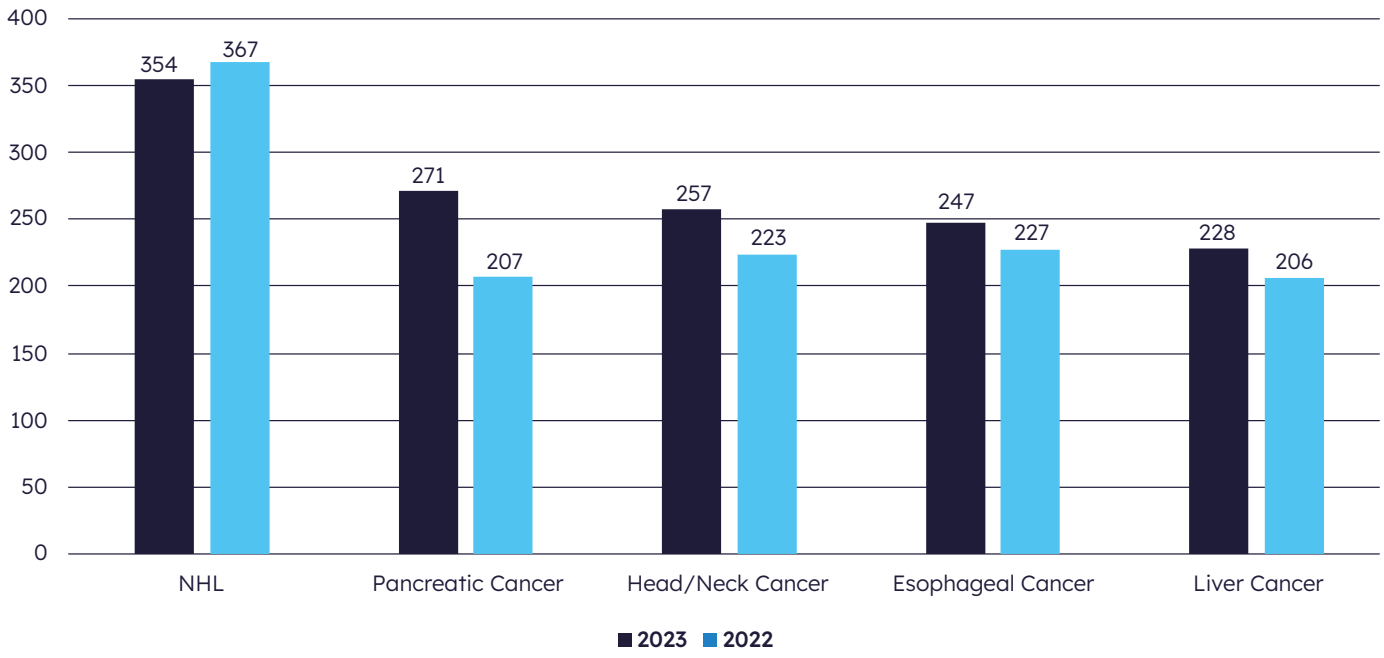
Figure 4: Rare disease trial initiations in Phase I–III, 2011–23



Source: Trialtrove, June 2024

Our past surveys of the rare disease trial landscape pointed to the oncology TA being where the most research efforts reside, and this year is no different. The top five rare diseases in Figure 5 happened to be the same top five we featured in the previous edition. Historically, NHL has been the top rare disease, but in 2023 it is the only indication in the top five that decreased in trial number, whereas the other four all experienced modest increases, with pancreatic cancer having the largest differential.

Figure 5: Top five indications in rare diseases, by trial initiations, 2022–23



Source: Trialtrove, June 2024

If we turn our focus on rare diseases outside of the oncology TA, Table 4 shows quite a diversified portfolio and tighter competition among the top 10.

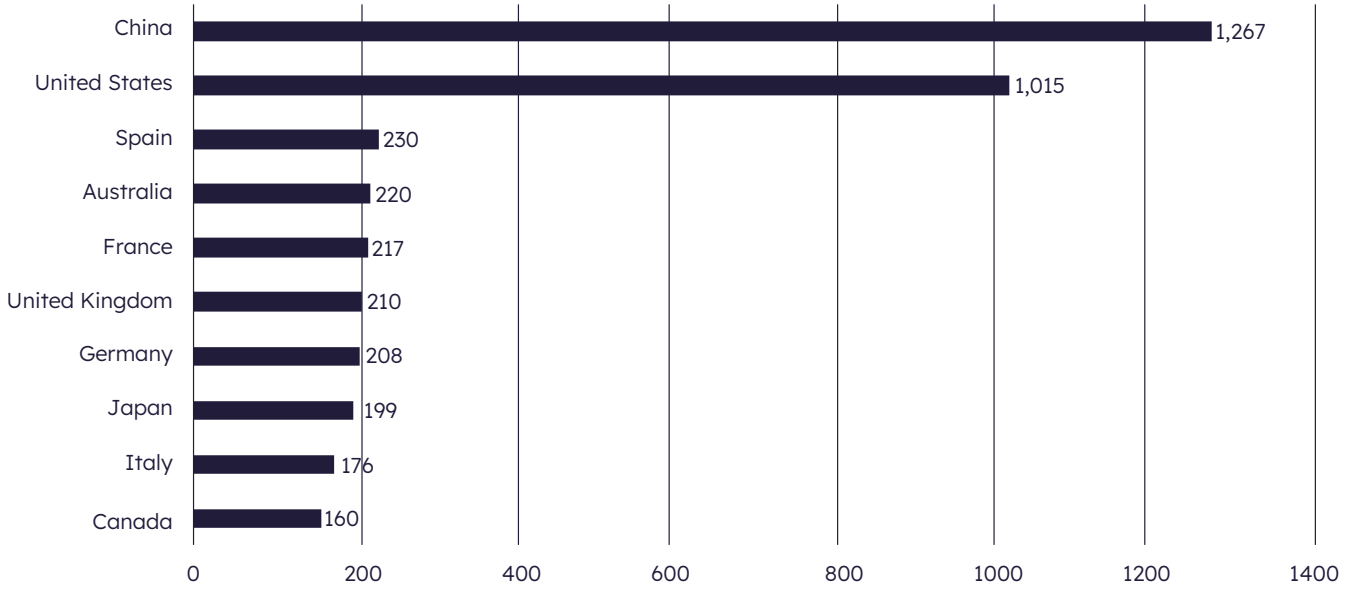
Table 4: Top 10 rare diseases in non-oncology TAs by trial initiations, 2023

Disease	# of trials 2023 (2022)
Immune Thrombocytopenia (ITP)	45 (25)
Tuberculosis (TB)	43 (33)
Pulmonary Hypertension	39 (NA)
Amyotrophic Lateral Sclerosis	28 (35)
Muscular Dystrophy	24 (24)
Thalassemia	23 (13)
Cystic Fibrosis	22 (26)
Sickle Cell Disease	22 (28)
Dermatomyositis/Polymyositis	16 (NA)
Scleroderma	16 (20)

Source: Trialtrove, June 2024

The geographical landscape of rare disease trials in Figure 6 highlights China's persistent dominance in this space, given its strong focus in the oncology TA.

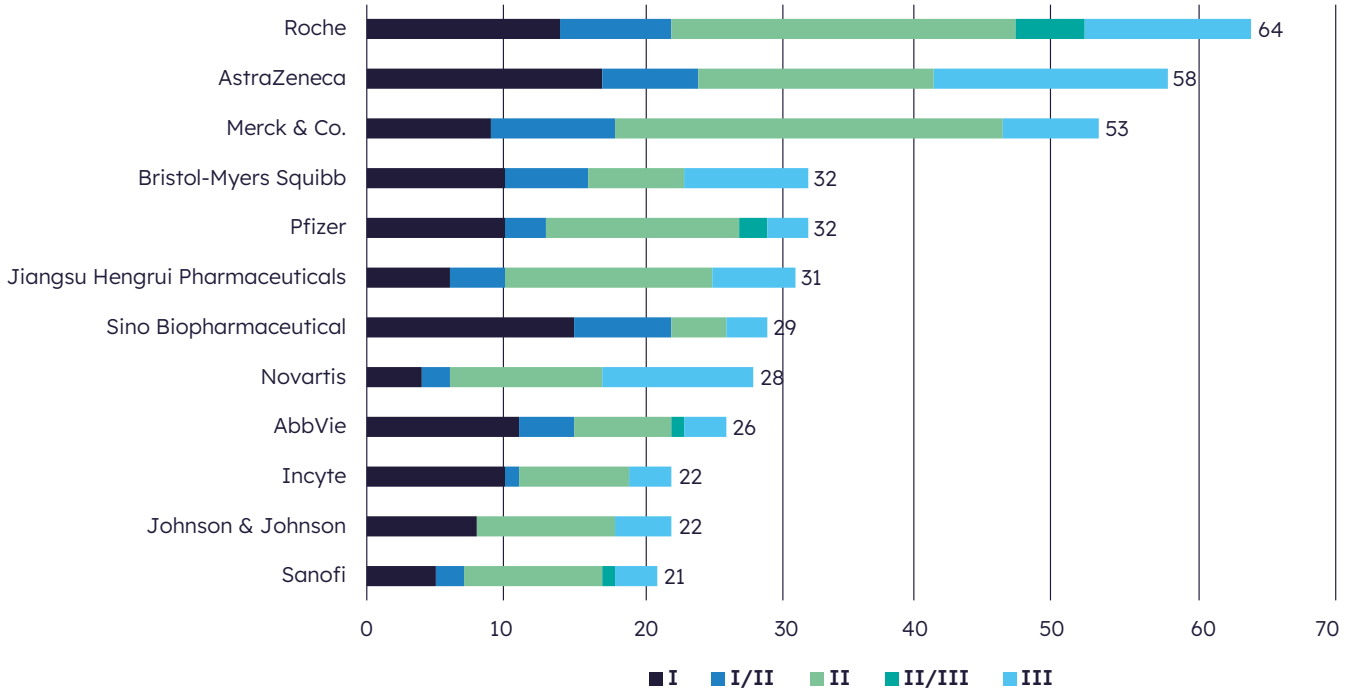
Figure 6: Top 10 countries of rare disease clinical trials in 2023



Source: Trialtrove, June 2024

However, the top industry sponsors of rare disease trials in Figure 7 shows the top five spots are filled by western top 20 pharma companies, with only two Chinese companies, Jiangsu Hengrui and Sino Biopharmaceutical, exerting their presence within the top 10. This landscape reflects the impact of China's National Medical Products Administration (NMPA) reforms that incentivize foreign drug development and clinical trials.

Figure 7: Top industry sponsors in rare disease clinical trials, 2023



Source: Trialtrove, June 2024

The growing importance of rare diseases has pulled together community lobbyists, patient advocates, and drug developers, driving the influence behind the US FDA's creation of the rare disease "hub," which will act as a Center of Excellence, much like the Oncology Center of Excellence that the FDA instituted in 2016.[5] The hub will aim to provide needed regulatory flexibility for rare disease drug development. The decrease in trial initiations during 2023 may seem to hinder post-pandemic recovery, but the hub's emergence could reignite momentum. Rare disease R&D remains a strong focus in the healthcare industry because of the debilitating nature of these conditions. The number of targeted rare diseases continues to rise, reaching 761 in 2023, as reported by Citeline's Pharma R&D Annual Review 2024.[2] This translates to a 7.6% rise in the number of drugs under development from the prior year, representing 30% of all drugs in the pipeline.

5. Citeline (2024) US FDA Creating Rare Disease 'Hub' To Serve As Center Of Excellence

Key Industry Sponsors in 2023 Trial Initiations

The top 10 industry sponsors maintained a relatively stable composition with minor rank fluctuations until 2023, when a more dynamic landscape emerged. AstraZeneca regained its crown with 139 trials after it was edged down by Merck & Co. in 2022 (Table 5). Pfizer climbed to the second position with 128 trials, a significant ascent from its consistent mid-table ranking in previous years, narrowly outpacing last year's champion Merck & Co., as well as Roche. Merck & Co.'s decrease in Phase II trials led to the loss of its No. 1 position (Figure 8).

Chinese pharma company Jiangsu Hengrui Pharmaceuticals continued its mid-tier standing among the top 10. 2023 welcomed a newcomer to the top 10, Sino Biopharmaceutical, which overtook two top 10 pharma companies, Novartis and Johnson & Johnson. Eli Lilly climbed up two positions from its customary lower echelon of the top 10 pharmaceutical companies, a trajectory undoubtedly accelerated by the success of its tirzepatide and donanemab programs.

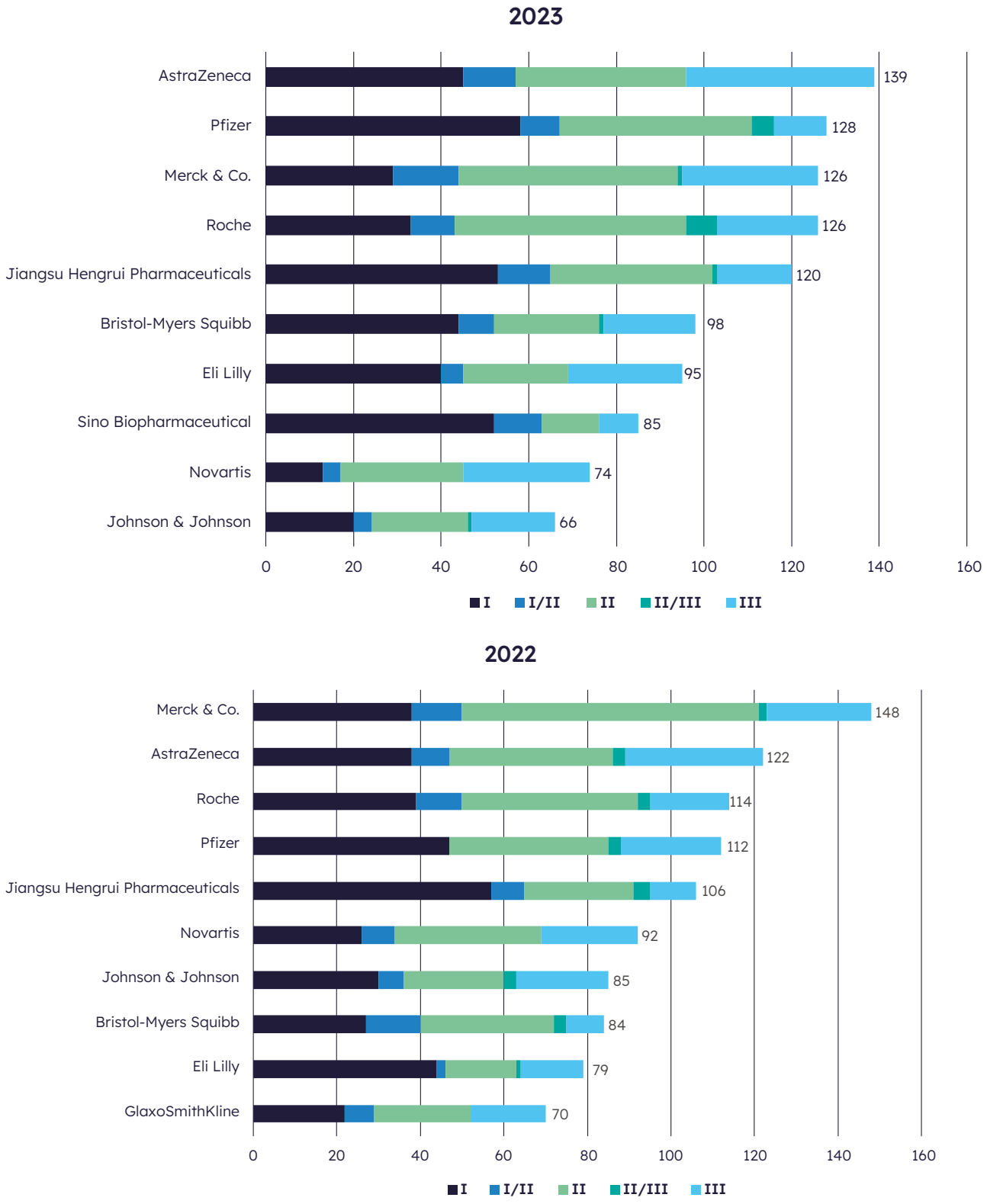
Table 5: Rankings of top 10 industry trial sponsors, 2023

Sponsor	Rank 2023 (2022)	# of trials 2023 (2022)
AstraZeneca	1 (2)	139 (122)
Pfizer	2 (4)	128 (112)
Merck & Co.	3 (1)	126 (148)
Roche	3 (3)	126 (114)
Jiangsu Hengrui Pharmaceuticals	5 (5)	120 (106)
Bristol-Myers Squibb	6 (8)	98 (84)
Eli Lilly	7 (9)	95 (79)
Sino Biopharmaceutical	8 (11)	85 (61)
Novartis	9 (6)	74 (92)
Johnson & Johnson	10 (7)	66 (85)

Source: Trialtrove, June 2024

Trial distributions across Phase I–III development among the top 10 sponsors revealed that Pfizer had the most Phase I trials (58 trials), followed closely by Chinese companies Jiangsu Hengrui (53 trials) and Sino Biopharmaceutical (52 trials). Earlier, Figure 2A revealed that Phase I trials comprised over 44% of all trial initiations in 2023; consequently, it is unsurprising that they dominate trial activity among the top 10 industry sponsors. Roche and Merck & Co. led with the most Phase II trials, which were primarily dedicated to the oncology TA. AstraZeneca reigned in Phase III trial initiations in both 2022 (33 trials) and 2023 (43 trials).

Figure 8: Top 10 industry sponsors by trial distributions in Phase I–III, 2022–23



Source: Trialtrove, June 2024

Top Disease Focus by 10 Most Active Sponsors

We now examine the primary disease focus of the top 10 sponsors in detail, comparing their ongoing commitments with any shifts in direction. Table 6 summarizes the top three diseases for each of the top 10 industry sponsors in 2022 and 2023. The number of unique diseases has bounced between 17 and 22 over the last five years, with 16 being the final number in 2023. The diminished diversity in disease portfolios indicates converging or renewed competition in some disease areas, as the pandemic no longer influences the primary disease landscape here. Previously, we saw six out of the top 10 sponsors retain their No. 1 disease, whereas this year only Novartis and Johnson & Johnson kept their No.1 commitment unchanged, in breast cancer and multiple myeloma, respectively.

The overwhelming presence of oncological diseases continues to be evident among the top 10 industry sponsors. Companies like AstraZeneca, Merck & Co., Roche, Jiangsu Hengrui, Bristol Myers Squibb, and Sino Biopharmaceutical all have robust oncology pipelines to sustain their top-ranking status. NSCLC remains the highest priority disease among the top 10 sponsors, followed by unspecified solid tumor and breast cancer. Nearly all companies prioritized oncology as one of their top three therapeutic areas for clinical trials in 2023. Eli Lilly diverged from the trend with its steadfast commitment to obesity, T2D, and dyslipidemia in both years. Following the containment of the pandemic, Pfizer invested in oncology with its Seagen acquisition, which enabled it to inherit active clinical programs of tucatinib in breast cancer.

Consistency is a hallmark of top sponsors, with at least two of their top three diseases typically unchanged. Johnson & Johnson stood out this time as it diverged from a diversified TA portfolio to increase its footprint in the oncology TA.

Table 6: Top diseases by the most active sponsors, 2023 vs. 2022

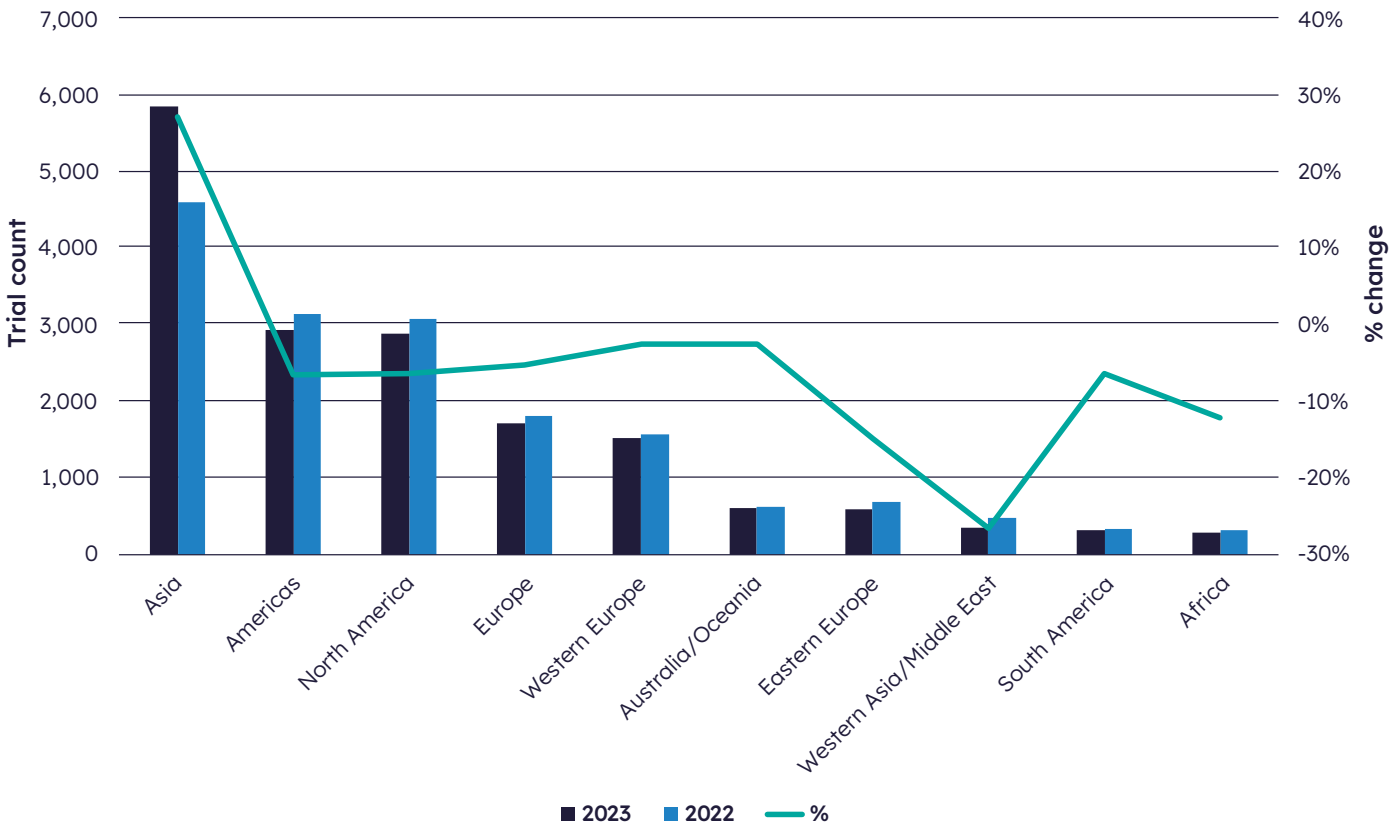
Top diseases by trial volume				
Company	**Year**	**#1**	**#2**	**#3**
AstraZeneca	2023	Breast cancer (14)	NSCLC (12)	Bile duct cancer (9)
	2022	NSCLC (18)	breast cancer(10)	COPD (7)
Pfizer	2023	Respiratory Infections (22)	Breast cancer (19)	COVID-19 (10)
	2022	COVID-19 (20)	Respiratory Infections (15)	Respiratory Vaccines (10)
Merck & Co.	2023	NSCLC (19)	Unspecified Solid Tumor (13)	Renal cancer (12)
	2022	Unspecified Solid Tumor (18)	Colorectal (15)	NSCLC (13)
Roche	2023	NSCLC (17)	NHL (15)	Unspecified Solid Tumor (14)
	2022	NHL (14)	NSCLC (11)	Liver cancer (9)
Jiangsu Hengrui Pharmaceuticals	2023	Type 2 Diabetes (15)	Unspecified Solid Tumor (13)	Breast cancer (12)
	2022	Unspecified Solid Tumor (18)	Breast cancer (13)	Pain, nociceptive (12)
Bristol-Myers Squibb	2023	NSCLC (12)	Unspecified Solid Tumor (9)	Colorectal cancer (7)
	2022	Unspecified Solid Tumor (11)	NSCLC (8)	Renal cancer (8)
Eli Lilly	2023	Obesity (26)	Type 2 Diabetes (26)	Dyslipidemia (10)
	2022	Type 2 Diabetes (13)	Obesity (10)	Dyslipidemia (7)
Sino Biopharmaceutical	2023	NSCLC (9)	Unspecified Solid Tumor (8)	Breast cancer (7)
	2022	Unspecified solid tumor (7)	NSCLC (6)	Unspecified cancer (5)
Novartis	2023	Breast cancer (7)	Dyslipidemia (5)	Urticaria; Renal disease: NSCLC; Prostate cancer; Unspecified solid cancer (4)
	2022	Breast cancer (13)	NSCLC (8)	Lupus (4)
Johnson & Johnson	2023	Multiple myeloma (13)	NSCLC (7)	Prostate cancer (7)
	2022	Multiple Myeloma (13)	Depression (7)	Psoriasis (5)

Source: Trialtrove, June 2024

Geographical Survey of Trial Activity

So far, we have surveyed 2023 trial initiations by their TAs, phases, diseases, and sponsors, and, of course, it is time to identify geographical powerhouses and regions experiencing decline. The last 10 years have witnessed a remarkable increase in clinical trials across Asia, with China as the primary driver, followed by Japan and South Korea. Figure 9 shows that globally, most regions experienced a modest decline in the number of trial initiations from 2022 to 2023, except for Asia, which enjoyed a significant surge. The percentage change view highlights a sharp decline in Western Asia/Middle East, where we will examine further to understand the impact of political conflicts on clinical trials.

Figure 9: Trial distribution by region, 2022–23

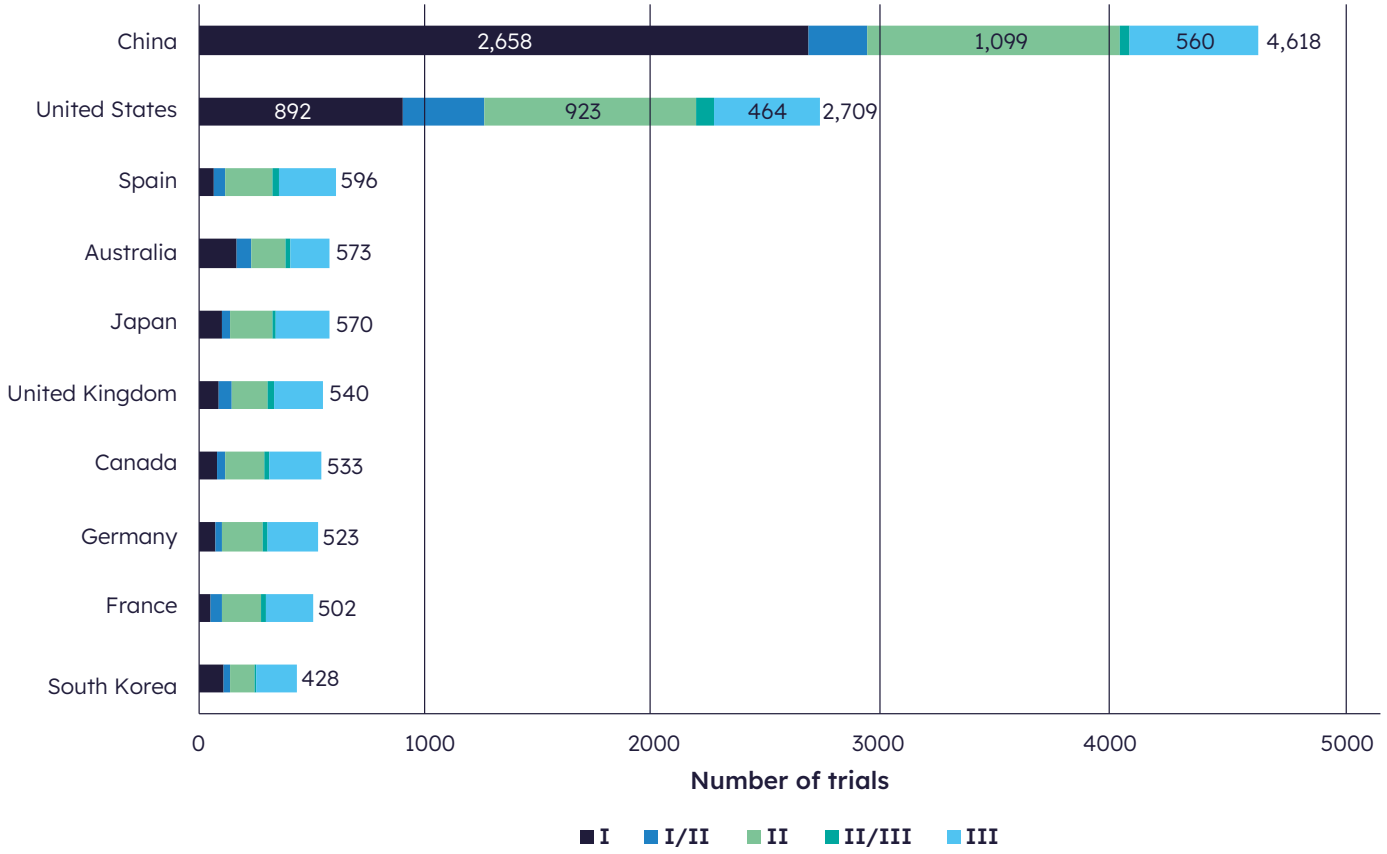


Source: Trialtrove, June 2024

For many years, the US had consistently reigned as the leading clinical trial market with China trailing closely behind. A significant shift occurred in 2021, when China overtook the US to become the leading market, a position it has held to date. Figure 10 highlights China's significant advantage, with Phase I trials as a key driver of its leading position. The US, on the other hand, has a more even distribution between Phase I and Phase II trials, while also sustaining a healthy portion of Phase III activities.

In general, Phase I trials represent a critical phase of drug development from the safety perspective, and there is a growing emphasis on transparency and data sharing in clinical research. However, it is important to be aware of specific country requirements for the reporting of Phase I trials. For example, FDAAA 801 in the US stipulates that Phase I trials are not subject to the mandatory reporting requirement, because drugs, medical devices, and biologics are regulated by the FDA. This contributes to a much smaller chunk of Phase I trials in the US compared to China. If we exclude Phase I trials from the picture, it would no doubt significantly shrink the trial volume gap between the US and China. The remaining eight countries reside in Europe, as well as Australia, Canada, Japan, and South Korea, all favoring mid-to-late-stage clinical trials.

Figure 10: Top 10 countries by volume of clinical trial initiations in 2023



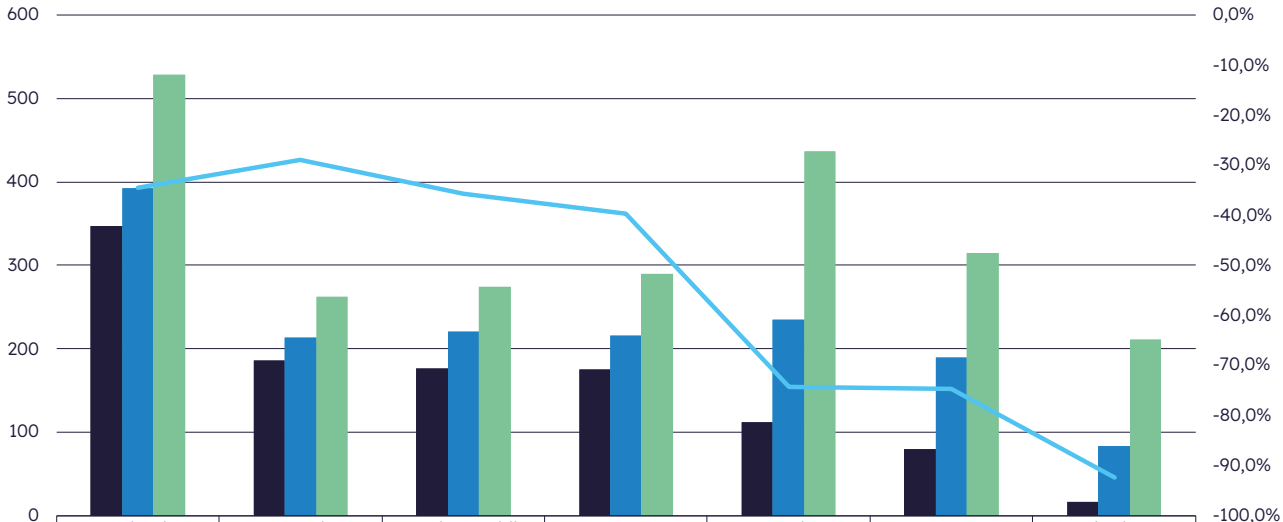
Source: Trialtrove, June 2024

In our last edition of this review, we began to evaluate the impact of geopolitical conflicts on the clinical trials landscape, as some of the countries involved were up-and-coming hotbeds for clinical research. The war in Ukraine and Russia resulted in massive numbers of displaced patients, including facilities and investigators that are essential to maintain clinical trial operations. The year 2022 saw the number of trials plunge by more than 60% in Ukraine and by 46% in Russia. The ripple effect also caused trials in nearby countries like Poland and Hungary to drop by more than 25% as well.

Prior to the Russo-Ukrainian war, countries in Eastern Europe were promising stars for clinical trials. Figure 11 illustrates that the ongoing stalemate of the war led to further declines in clinical trials for Ukraine (-92.4%) and Russia (-74.4%) over 2021–23. As expected, the negative impact extended to neighboring countries, including Poland (-34.4%), Czech Republic (-35.8%), and Hungary (-39.7%).

On the gloomy note of war, the Hamas-Israel conflict in late 2023 overshadowed the war in Ukraine. Clinical trials in Israel dropped by 29% from 2021 to 2023; at the same time, the instability of the Gaza conflict impacted clinical trials in Iran at a near 75% decline. The downturn in these countries mirrored the slumps depicted for Eastern Europe and Western Asia/ Middle East in Figure 9.

Figure 11: Country-level trial numbers for countries in and near geopolitical conflicts, 2021–23



	Poland	Israel	Czech Republic	Hungary	Russia	Iran	Ukraine
2023	347	186	176	175	112	80	16
2022	393	213	220	216	235	190	83
2021	529	262	274	290	437	315	211
Delta 2021-23	-34.4%	-29.0%	-35.8%	-39.7%	-74.4%	-74.6%	-92.4%

Source: Trialtrove, June 2024

War has a devastating impact on healthcare infrastructure, as hospitals, clinics, and medical supply chains are often targeted and destroyed in conflict zones. The consequences are far-reaching and long-lasting, exacerbated by limited access to lifesaving medicines and a shortage of healthcare workers due to displacement. Recognizing the massive loss of clinical trial momentum, we intend to reassess the outlook for these countries next year.

Clinical Trials by Country and Therapeutic Areas

For many years we have assessed the trial landscape by locations and TAs. This part of the analysis explores the performance and challenges of TA activities across the leading trial countries. Table 7 provides a comparative analysis of the top 10 countries in terms of trial volumes and TAs. A quick survey across all charts establishes China's leading position in all TAs except OPH, where it ranked second behind the US. In every TA, either China or the US occupies the top two positions, with a significant lead over any runners-up behind them.

When we consider the overall trials, only Asian countries saw increased trial numbers, with China leading the pack and a much-improved standing for Japan. The US, Europe, Canada, and Australia make up the remaining top 10, and all had fewer trials in 2023. Australia moved up the rank (up from seventh to fourth), while the UK, Germany, and France all fell.

In the A/I TA, the UK made some headway, raising its number of trials from 110 to 147, bumping its standing from seventh to third rank. Respiratory indications like asthma, pulmonary fibrosis, and COPD are the main drivers that elevated the UK's standing in this TA.

Oncology is the largest TA for clinical trials, where over 81% of the trials reside either in the US or China. Meanwhile, there are minor shifts in ranking among the remaining eight countries, as Canada debuted in the top 10 this year, sharing the 10th rank with the UK.

Geographical distribution for CNS trials showed a dramatic climb for India, where pain trials elevated India's standing from 12th to third place. Germany and Spain also enjoyed a modest climb in ranking, while Australia and France fell a few positions lower.

The CVS TA had an interesting dynamic between the third to 10th standings. While there were no impressive changes in the number of trials, Japan, Germany, and Spain tied for fourth position with 47 trials each, and all moved up from the lower echelons compared to the prior year.

The success of T2D drug development picked up some momentum for the MET TA, where India and South Korea ascended through the ranks, overtaking Germany and the UK from the prior year.

The significant decline in COVID-19 trials brought a more dynamic landscape change in the ID TA. More trial initiations occurred in Japan and Canada in 2023, but numbers significantly declined in Spain.

The GU TA is one of the smaller TAs, and this year we see Spain, Taiwan, and the UK entering the top 10 in this TA. The OPH TA is the only TA where the US leads over China in trial numbers, and this year we see a tie among Australia, Japan, Canada, and India at the third ranking.

Table 7: Ranking of top 10 industry trial sponsors by trial volumes and TAs

Overall		
Country	2023 (rank)	2022 (rank)
China	4,618 (1)	3,405 (1)
US	2,709 (2)	2,876 (2)
Spain	596 (3)	644 (3)
Australia	573 (4)	577 (7)
Japan	570 (5)	530 (9)
UK	540 (6)	609 (4)
Canada	533 (7)	560 (8)
Germany	523 (8)	580 (6)
France	502 (9)	593 (5)
South Korea	428 (10)	422 (11)

Autoimmune/Inflammation		
Country	2023 (rank)	2022 (rank)
China	635 (1)	400 (1)
US	383 (2)	397 (2)
UK	147 (3)	110 (7)
Germany	140 (4)	132 (3)
Canada	140 (4)	122 (5)
Spain	137 (6)	122 (6)
Poland	124 (7)	125 (4)
Japan	118 (8)	100 (8)
Australia	116 (9)	91 (10)
France	115 (10)	92 (9)

Oncology		
Country	2023 (rank)	2022 (rank)
China	1,804 (1)	1,492 (1)
US	1,221 (2)	1,256 (2)
Australia	258 (3)	226 (5)
Spain	255 (4)	267 (4)
France	230 (5)	270 (3)
Japan	214 (6)	207 (7)
Italy	195 (7)	203 (8)
South Korea	190 (8)	191 (10)
Germany	185 (9)	202 (9)
Canada	169 (10)	183 (11)
UK	169 (10)	219 (6)

CNS		
Country	2023 (rank)	2022 (rank)
China	569 (1)	388 (2)
US	413 (2)	511 (1)
India	86 (3)	63 (12)
UK	75 (4)	100 (5)
Canada	70 (5)	106 (3)
Spain	70 (5)	87 (7)
Germany	69 (7)	77 (10)
Australia	66 (8)	102 (4)
Japan	64 (9)	85 (8)
France	58 (10)	90 (6)

Cardiovascular		
Country	2023 (rank)	2022 (rank)
China	551 (1)	309 (1)
US	149 (2)	146 (2)
UK	49 (3)	44 (6)
Japan	47 (4)	42 (7)
Germany	47 (4)	41 (9)
Spain	47 (4)	40 (10)
Canada	46 (7)	54 (3)
South Korea	43 (8)	49 (4)
Australia	43 (9)	38 (11)
France	42 (10)	41 (8)

Metabolic/Endocrinology		
Country	2023 (rank)	2022 (rank)
China	565 (1)	403 (1)
US	284 (2)	277 (2)
India	91 (3)	73 (5)
South Korea	81 (4)	62 (8)
Canada	74 (5)	69 (6)
Japan	72 (6)	73 (5)
Germany	64 (7)	76 (3)
UK	63 (8)	74 (4)
Australia	58 (9)	58 (10)
Spain	55 (10)	62 (9)

Infectious Disease		
Country	2023 (rank)	2022 (rank)
China	469 (1)	416 (1)
US	264 (2)	304 (2)
Japan	56 (3)	47 (9)
India	52 (4)	74 (3)
Australia	52 (4)	72 (5)
UK	52 (4)	70 (6)
Canada	46 (7)	34 (12)
South Africa	45 (8)	59 (8)
Spain	44 (9)	74 (3)
France	38 (10)	47 (9)

Genitourinary		
Country	2023 (rank)	2022 (rank)
China	133 (1)	65 (1)
US	19 (2)	24 (2)
Iran	19 (2)	13 (3)
India	14 (4)	11 (4)
Egypt	14 (4)	9 (5)
Japan	10 (6)	7 (6)
Spain	7 (7)	4 (11)
Taiwan	5 (8)	0
UK	5 (8)	3 (12)
Germany	4 (10)	7 (6)

Ophthalmology		
Country	2023 (rank)	2022 (rank)
US	89 (1)	74 (1)
China	59 (2)	40 (2)
Australia	11 (3)	13 (3)
Japan	11 (3)	10 (4)
Canada	11 (3)	6 (9)
India	11 (3)	6 (9)
Spain	10 (7)	9 (5)
Germany	10 (7)	7 (8)
South Korea	9 (9)	3 (15)
UK	8 (10)	6 (9)

Source: Trialtrove, June 2024

Overall, we will likely see China and the US continue to occupy the top two positions across all TAs because their lead over the other countries is quite remarkable, leaving a big gap for any other country to fill. Stability in the top 10 locations of each TA appeared to be well maintained. A few highlights included Japan's advancement in ID and CVS, as well as India's growing prominence in CNS and OPH.

Clinical Trials Outlook in the Age of AI, Diversity, and Innovative Designs

The COVID-19 pandemic served as a catalyst to highlight critical issues of traditional clinical trial methodologies. These challenges are amplified by existing difficulties including limited funding, pricing pressures in major markets, heightened regulatory hurdles, and supply chain vulnerabilities. The clinical trial landscape has been on a roller-coaster ride over the last four years. Last year we recognized the struggle of the biopharma industry that operated in survival mode, and the present analysis is showing signs of gradual recovery as the number of trials is again on the upswing.

Recent advancements in clinical trial frameworks have propelled a paradigm shift to usher in a new era of innovation and efficiency. Let us look at some of the ways that the biopharma industry is adapting to modernize clinical trials. Concepts like patient-centricity, decentralized clinical trials (DCT), real-world data, artificial intelligence (AI), synthetic or historical controls, and innovative protocol designs are at the forefront of healthcare industry discussion.

Patient voices and trial sites are increasingly recognized as essential partners in clinical trials. One of the largest pain points here is patient recruitment, not only in finding the most suitable candidates for the study and achieving target enrollment, but also retaining their participation through study completion. Some studies implement patient-centered incentives, such as flexible visit schedules, transportation assistance, childcare support, and cultural accommodations, all aiming to reduce the recruitment barrier. These approaches work synergistically to help the trial sponsors fulfill FDA requirements on diversity action plans.

The idea of patient-centricity is inextricably linked to the adoption of DCT, because the majority of DCT attributes enable greater patient flexibility and access, improved enrollment and retention, and empowerment of DE&I. However, the benefits of DCT are complicated by regulatory harmonization across countries, especially for sponsors that run global trials. Other challenges like data integration from multiple platforms, data security issues, and site enablement to minimize learning curves associated with new technologies contribute to a slow adoption of DCT elements.[6] This behavior aligns with the famous Kübler-Ross change curve, fluctuating between frustration and experimentation stages, before the final, upward curve to resurgence. Given the current trajectory, DCT are likely to become increasingly prevalent, and we anticipate significant advancements soon. We surveyed the 2023 trial initiations that were curated with a DCT element in Table 8, showing the top TAs that embraced DCT elements are CNS (29%), MET (20%), and ID (22%). While academics once led the way in DCT, industry sponsors have made significant strides in recent years. DCT usage remains most prevalent in North America, and particularly in Phase II studies (44%).

Protocol optimization is also a key area of innovation in clinical trials, with novel designs aimed at increasing efficiency. We are seeing an increasing trend of platform trials, as well as trials incorporating adaptive design, basket and umbrella elements, and sometimes a combination of these. There is also more emphasis on dose optimization that aims to

6. Citeline (2023) Unlocking the Potential of Decentralized Clinical Trials

refine the doses instead of maximizing them. Synthetic control arms and historical controls are emerging as innovative approaches in clinical trials. They offer the potential to eliminate traditional placebo control arms, reduce patient recruitment cost, and ensure that all patients benefit from treatment, particularly in debilitating diseases. We systematically analyzed 2023 trial descriptions based on keywords related to design and innovation to identify trials employing novel approaches. Table 8 reveals that over 68% of trials adopting innovative designs reside in the oncology TA, and industry sponsorship makes up about 77% of these trials. The US, Spain, and the UK are the top locations where we find these trials.

A major game changer across various sectors, including clinical research, is undoubtedly the rise of AI. The advantages and risks associated with the applications of AI and machine learning (ML) in clinical research continue to be hot topics. A recent Citeline article discussed the exponential rise in the use of AI in drug development submissions and the emerging success of AI-driven drug discovery.[7] The paper also elaborated on pain points associated with AI adoption which we will not delve into here. We applied text mining searches of relevant keywords to 2023 trials (Table 8), which indicated that about 58% of trials that adopted AI/ML models reside in oncology. The main sponsor type is associated with the "Industry, all other pharma" category, and the US is at the forefront of AI/ML exploration. While AI/ML is widely used in drug development and regulatory submissions, the number of publicly disclosed clinical trials leveraging these technologies remains relatively small. Despite potential challenges, AI's undeniable potential justifies continued R&D.

Table 8: Phase I–III clinical trials attributed with elements of DCT, innovative trial designs, and AI/ML adoptions, 2023

Total trials	DCT	241	Innovative designs	324	Artificial Intelligence (AI)	38
Top TAs	CNS	71	Oncology	221	Oncology	22
	ID	52	CNS	33	CNS	9
	MET	48	ID	33	A/I	5
Sponsor type	Academic	117	Industry, all other pharma	167	Industry, all other pharma	24
	Industry, all other pharma	88	Academic	130	Academic	15
	Industry, Top 20 Pharma	47	Industry, Top 20 Pharma	85	Government	8
Top countries	United States	114	United States	205	United States	23
	UK	37	Spain	53	China	8
	Canada	34	UK	49	Canada, Spain	4
Phase	II	106	II	114	I	12
	III	56	I	94	II	12
	I	45	I/II	66	I/II; III	5

Source: Trialtrove, June 2024

7. Citeline (2024) The Promise and Peril of AI in Clinical Trials

Concluding Thoughts

The robust growth of clinical trial initiations in 2023 signals a promising revival following last year's decline. The complex landscape of clinical trials is fraught with pressures and risks, exacerbated by the industry's adoption of new technologies, regulatory burdens, and drug pricing negotiations. While many of these hurdles occur at the drug development stage, they inevitably also influence investment in new clinical trials. In 2022, there was a palpable sense of trepidation, but now we are witnessing signs of a brighter future. In the coming year, we anticipate further advancements in generative AI, improved efficiency through innovative trial design, and collaborative dialogue with regulatory authorities to illuminate the future of clinical trials.

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Heidi Chen supports client engagement with Citeline content through a deep understanding of customer business needs, seasoned expertise in proprietary platforms, market analysis, and commercial activities.

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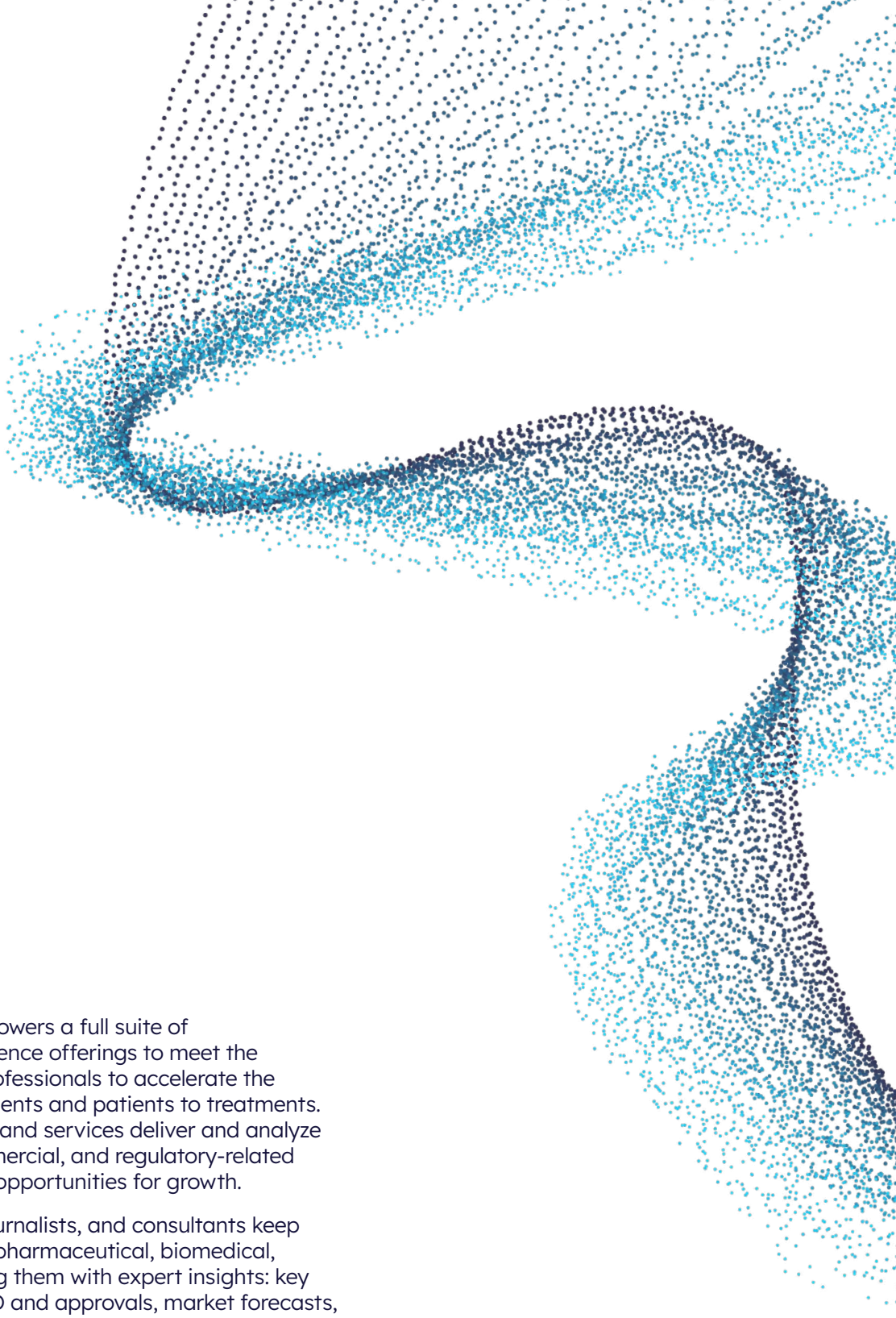

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