Assessing the clinical trial ecosystem in Europe

Final Report

October 2024

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Executive summary (1/4)

The European clinical trial ecosystem is critical to patients, healthcare systems and society:

- For patients, clinical trials offer early access to innovative medicines, and for rare disease patients, trials can be the only treatment option
- For health systems, clinical trials bring revenue, cost-savings, clinical skills, and staff satisfaction
- For society, clinical trials bring economic investment and GDP benefits, valued at multi-billion Euros

Recent European level and member state policy initiatives have attempted to increase the capabilities and attractiveness of the clinical trial ecosystem. For example, EU Clinical Trials Regulation (CTR) aimed to harmonize clinical trial capabilities across Europe, and make multi-country applications more streamlined, with the goal of boosting Europe's competitiveness in attracting clinical trials. This goal has not yet been met. At best, Europe has held, but not improved its position.

Our research suggests that whilst Europe is a strong performer in commercial multi-country clinical trials, it is losing global share, particularly to Asia and other regions (falling from 25% in 2013, to 19% in 2023). Similar trends are seen in total commercial trials (single and multi-country)

- The loss of share to China could be linked to a more favorable regulatory and funding environment for Phase 1 and Cell and Gene Therapy trials, where Europe has seen a particular decline in trial starts. Late-stage clinical trials in China are often focused local/regional approvals, so may not be viewed as direct 'competition' to EEA and US performance.
- The loss of share to US could be driven by trial start-up timelines. This research suggests regulatory approval timelines are not the greatest differential between US and Europe, but instead, patient recruitment times in Europe may be impacting the attractiveness of Europe as a trial location. This is a multifaceted issue, but data access to enable patient-finding in niche populations could be restricting recruitment speed. However, it should be noted, most Western countries, including the US, are seeing a slow-down in clinical trial set-up and recruitment, likely reflecting increasing trial complexity, and challenges in finding suitable patients. Other factors influencing European vs. US trends include the varying levels of funding available to biotech, and wider M&A landscape, however this data have not been directly explored in this report.

As a result of the declining share of trials, Europe has also seen a fall of the global share of patients enrolled into clinical trials. Whilst patients enrolled in European trials grew slightly during the COVID-19 pandemic, it is estimated European patient enrollment has since fallen back to below pre-pandemic levels

Executive summary (2/4)

The decline in European performance is seen in key therapy areas, across phases, and commercial and non-commercial sponsors. For example:

- There has been a decline in the clinical trial starts for oncology, neurology, rare disease, immunisation and paediatric trials.
- Some reports suggest the In-vitro Diagnostic Regulation (IVDR), which introduced more stringent requirements for the designation of Notified Bodies and affected device risk classifications, pose operational challenges for multi-region trials in oncology (and other trials highly dependent on in-vitro testing). The implications of this regulation on clinical trial activity should be closely monitored. Similarly, whilst this research focuses on trends in pharmaceutical and vaccine trials, the impact of Medical Device Regulation (MDR) on the clinical trial ecosystem should also be observed, given their relevance to clinical trial delivery.
- Europe has seen a particular decline in the proportion of Phase 1 trials. Whilst Phase 2 and 3 trials may be considered more directly impactful for patients, a reduction in Phase 1 trials could lead to a reduced 'pipeline' of future trials in Europe. This is particularly relevant where specialized knowledge or equipment is developed during Phase 1, which supports continued delivery of later phases.
- Europe has seen a small decline in its share of commercially-sponsored clinical trials, compared to non-commercial sponsors (49% to 47% commercial share between 2018 and 2023). This represents a comparable share and trend to the US. However, our research shows declining European share in both sponsor-types, suggesting common challenges impacting both commercial and non-commercial sponsors.

In response to the COVID-19 pandemic and wider advances in vaccine technology, immunisation products and their associated clinical trials are a particular area of focus for global policy makers.

- Denmark and Spain have experienced an increase in the number of immunisation trials since 2018, following a similar trend (though not as pronounced) as the rise observed in the UK during the same period. However, in 2023, overall European immunisation trial activity fell back below pre-pandemic levels, contrasting to growth in other regions. The fall in Europe appears to be driven by a decline in Phase 3 and 4 trials in this therapy area, with a geographic shift towards China and Australia.

Executive summary (3/4)

Across European member states, performance is more nuanced:

- Spain has become the leading country for clinical trial starts in Europe, with a strong performance across most dimensions measured in this report. In Spain, over the past decade, the industry investment in clinical trials has risen at an average annual rate of 5.7%, climbing from EUR 479 million in 2012 to EUR 834 million in 2022. Factors attracting investment may include the capabilities of Spain's healthcare system, the successful and timely implementation of CTR (involving cross-stakeholder coordination and measurement), and an effective commercial/non-commercial clinical trial collaboration model. Notably, Barcelona hosts a major 'Prime Site' for clinical trials in Southern Europe, which has delivered increasing number of clinical trials since 2018, and plays a major role in Spain's clinical trial ecosystem.

- Meanwhile, many other European countries have seen a decline in clinical trial starts in 2023 vs. 2018. Germany has seen a decline in clinical trial starts, which has in part, been attributed to extensive negotiation times between companies and research institutions, and highly stringent data protection laws which may slow patient recruitment. Belgium has also seen a decline in trials, particularly in vaccine trials, an area in which it has historically performed strongly. Concerns regarding regulatory and ethical approval timelines, and reduced consultation with Principal Investigators have been raised by major Belgian trial centers.

Taken together, there has been a shift in trial starts from Northern and Western Europe, towards Southern Europe, with Spain, Portugal and Greece showing strong relative performance

Executive summary (4/4)

Europe remains a strong global player in clinical trials and has many strengths to build on. Whilst more time is required to assess the full impact of CTR, certain actions should be considered now:

- **Sustain or increase government funding into health R&D and support full adoption of CTR across member states**, through co-ordination of regulatory and ethical approval processes, and practical guidance derived from real-world experience**.** Our research suggests government investment and policy levers are important to attracting private sector investment into clinical trial infrastructure and operations, which subsequently provides benefits to patients, healthcare systems, and supports economic growth.
- **Action should be taken ensure approvals, site-start up, and recruitment speeds do not fall further**, which could increase the 'competitive-gap' with the US. This a multi-faceted challenge, and requires a thorough, country-level and EU-level assessment, with a multi-stakeholder delivery. Whilst in-depth analysis is required to identify specific bottlenecks, a range of factors are seen to enhance the clinical trial ecosystem:
    - From a policy perspective, minimizing regulatory complexity, and simplifying & harmonizing contracting processes
    - Tackling clinical trial capacity & infrastructure bottlenecks, by improving site readiness, addressing staffing constraints, and reducing the variability in health system awareness of clinical trials, given the negative impacts on recruitment rates
    - Leveraging novel, patient-centric clinical trial designs to improve delivery efficiency whilst increasing attractiveness to patients
- **Lessons should be taken from Spain's strong performance**, which is built on a cycle of early policy adoption embracing the 'spirit' and 'letter' of CTR, achieved via cross-stakeholder coordination, investment in major clinical trial sites, and strong commercial/non-commercial collaboration.

Tentative recommendations to EU law-makers:

The full impact of Clinical Trial Regulation is yet to be established, however, CTR has so far failed to improve Europe's competitiveness, and there are continued challenges with CTIS implementation . Despite the ambition of harmonized standards and common procedures for regulatory and ethical approvals, the capacity and motivation at member state level to implement these changes is inconsistent. Future EU and members state funding should focus on creating "ready-to-go" clinical trial networks, that are open to working with the private sector, to attract clinical trials to Europe.

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EFPIA & Vaccines Europe (VE) sought to measure the current clinical trial ecosystem and assess its impact in Europe, to inform future policy

Background to this project

- Clinical trials are key to driving innovation, with important impacts for patients, healthcare systems, researchers and associated R&D investment
- There is a desire across EFPIA and Vaccines Europe stakeholders to enhance European clinical trial capacity and become a hub for smarter, faster and more patient-centric trials
- However, there has been a lack of European-wide information, with suitable breadth and data granularity, to set a baseline measurement on EU clinical trial strategy and operational efficiency and to allow EU policymakers to assess policy opportunities and risks

Objectives

Therefore, IQVIA worked with EFPIA and VE to measure the impact of clinical trials in Europe and inform policy and operational recommendations by:

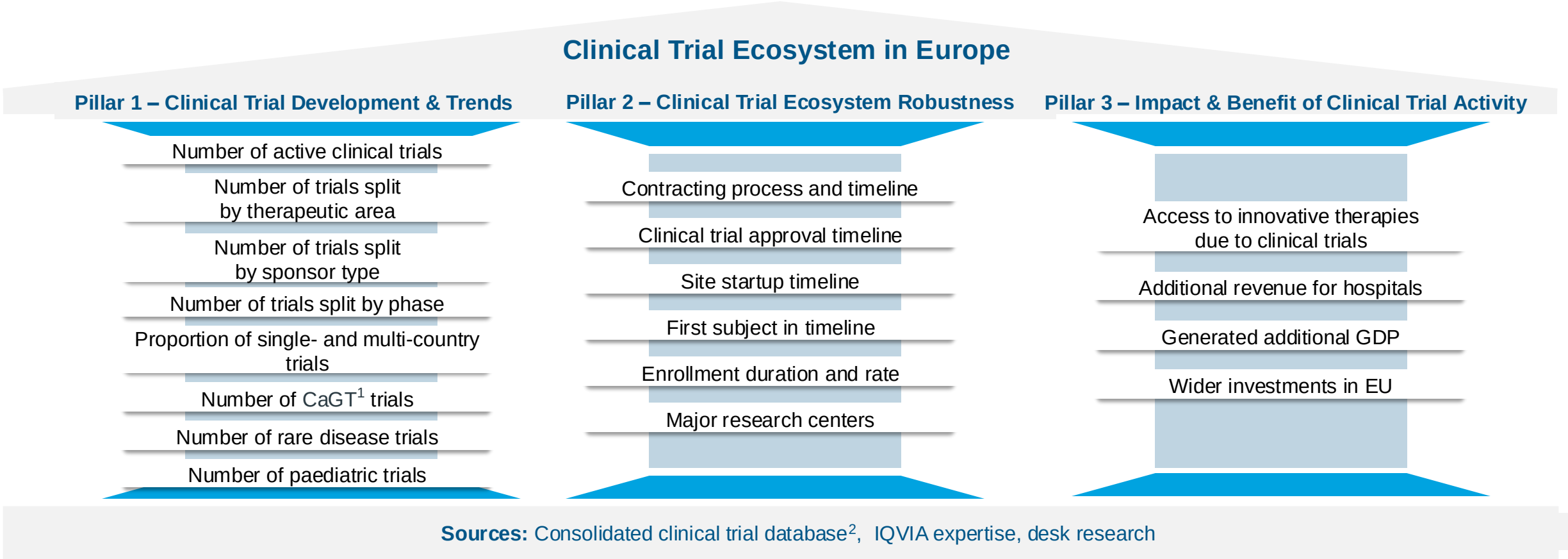
Establishing a baseline to measure policy impacts

- Create a picture of current clinical trial development and trial trends including comparisons to other key regions
- Use proxies and case studies to measure the clinical trial ecosystem robustness in Europe

Measuring the impact of clinical trials on patients, research and healthcare systems

- Use a range of proxies and case examples to demonstrate the importance and impact of the clinical trial ecosystem in Europe

The clinical trial ecosystem has been assessed through three pillars, each comprising of qualitative and quantitative metrics



Sources: Consolidated clinical trial database[2], IQVIA expertise, desk research

1. Cell and Gene Therapies
2 CT.gov, EudraCT (EU), UMIN (Japan), ISRCTN (global), ANZCTR (Australia, New Zealand), IRCT (Iran), NTR(Netherlands), HKCT (Hong Kong CTR) and DRKS (Germany) ChiCTR (China), JapicCTI (Japan), CTRI (India), CRiS (Korea), NMRR (Malaysia), HSA CTR (Singapore),JMACCT CTR (Japan), ReBec (Brazil), PHRR (Philippines), TCTR (Thailand), SRM CTR (Russia), Mexico CTR (Mexico), LCTR (Sri Lanka), PACTR (Pan African), RPCEC (Cuba)

The selected metrics allow a comprehensive assessment of the European ecosystem, in the context of global competition (1/2)

Geographical definitions

- Unless specified otherwise, Europe refers to EEA. Ex-EEA countries are included in 'Other European Countries'
- EEA countries: Austria, Belgium, Bulgaria, Croatia, Republic of Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Netherlands, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, Iceland, Liechtenstein and Norway
- Note: for regional-level analysis, multi-country EEA trials are counted once in the EEA total

Comparator countries

- Switzerland and UK: co-located, non-EU countries
- Australia and Canada: high-income, non-European countries
- US and Japan: major global pharma markets
- China, South Korea: major emerging pharma markets

Trial phase split

- Phase 2 includes Phase 1/2, Phase 2a, Phase 2b
- Phase 3 includes Phase 2/3

Sponsor type split

- Non-commercial
- Commercial: small emerging biopharma (EBPs), EBPs, large EBPs, mid pharma, large pharma
- Combined: both commercial and non-commercial sponsors

Clinical trials excluded from the assessment

- Medical devices trials (trials labelled as 'device' were excluded from the assessment, empty values were included)
- Suspended and terminated trials (trial labels within 'recruitment status')

The selected metrics allow a comprehensive assessment of the European ecosystem, in the context of global competition (2/2)

Trial initiation date ranges selection

- 2013: 'study start date' between 01/01/2013 and 31/12/2013; no filter on study end date
- 2018-2023: 'study start date' between 01/01/2018 and 31/12/2023; no filter on study end date

Paediatric trials

- Sub-population of all paediatric trials with participants 0-18 years of age only
- Trials including adult populations are excluded

Clinical trial timelines

- Approval, set-up and enrolment timeline estimated based on a cohort of IQVIA-conducted clinical trials; this provides a large dataset for reference, but may not be fully representative of global trends

'Immunisation' trial definition

- Infectious disease prophylactic vaccines (e.g., flu)
- Infectious disease therapeutic vaccines (e.g., HBV)
- Infection-related cancer vaccines, both therapeutic (e.g., CMV+ glioblastoma) and prophylactic (e.g., HPV)
- Infectious diseases prophylactic mAbs (e.g., RSV)

Between 2020-22, trials for COVID-19 treatments had a significant impact on immunisation trends, with varying impact across geographies

All data accurate as of data access in April-May 2024. Clinical trial registries are subject to regular revision and updates, with greatest likelihood of revision for trials stating in most recent year e.g., 2023

Certain caveats should be considered when interpreting the data in this report

1 Data quality and completeness

Source data for this report is drawn from 22 clinical trial registries. While every effort has been made to ensure the accuracy of this data, the following limitations are known:

- The registries **may not capture every trial**
- Meta-data about trials may be **retrospectively adjusted**, if new information is received by the registry
- **Trial classification** (across dimensions such as phase, location, sponsor type) **is subject to a degree of uncertainty**.
  - For example, sponsor type analysis is based on the primary sponsor, and where possible, information on the secondary sponsor is considered. However, **absolute values should be interpreted with a degree of caution, particularly when assessing small n= numbers**

2 Comparison of trial totals, across dimensions

Due to the calculation methodology, the comparison of sums will not lead to the same value:

- For example, when totals are shown by **country/region** there is an 'artificial' inflation, because trials with sites in multiple countries/regions are counted more than once. This is intentional, to show the geographic spread.
- For **phase**, the totals are affected trials with dual phases (e.g. Ph2/3), and certain trials where phase is not coded
- For **sponsor-split**, we are again reliant on the sponsor coding; however not all trials are coded, and some are dual-coded
- For single vs. multi-country trials, a combination of these factors applies.

Despite these caveats, absolute values have been shown in this report to provide maximum transparency. However, the focus of the analyses is on time-series trends and relative shares, where many of the data limitations are mitigated.

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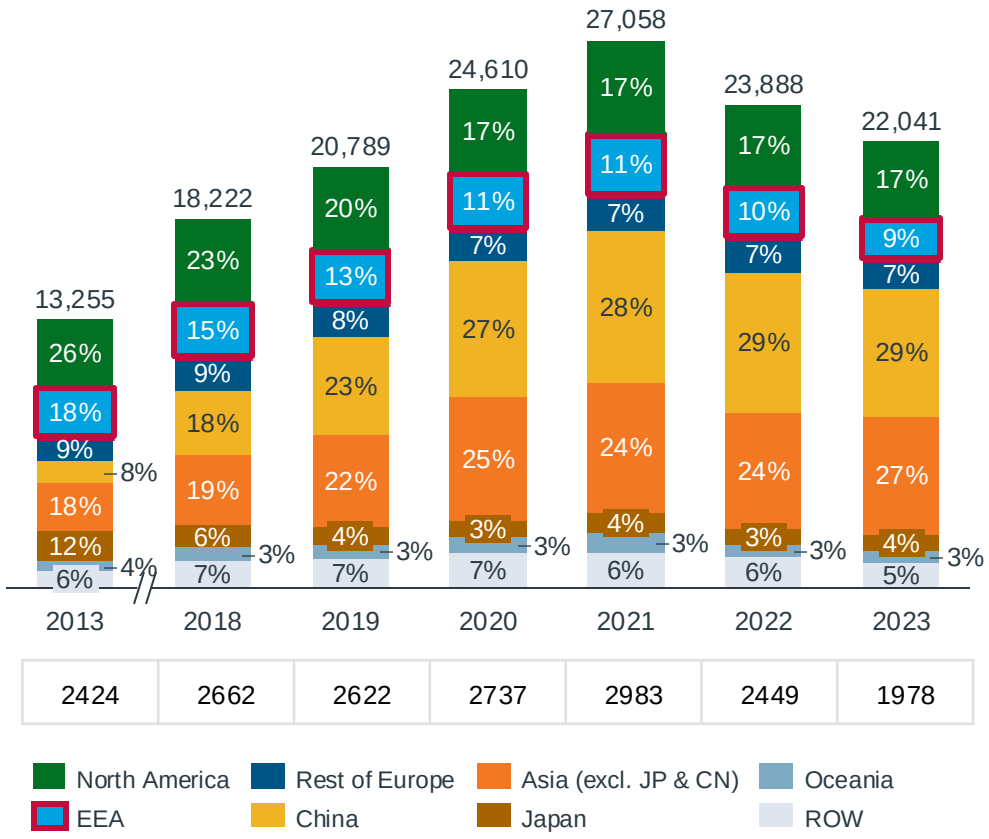
The global clinical trial ecosystem is evolving; Europe's share is declining, while Asia is emerging as a major location for new clinical trial starts

Number of global clinical trial starts by region (2013, 2018-2023; Phase 1-4)



Global trial starts grew year-on-year between 2013 and 2021. During this period, there has been a major evolution in geographical trial distribution. Post-2021, whilst absolute clinical trial starts have fallen back to pre-pandemic levels, relative geographic shares have remained broadly stable

- In 2013, North America, EEA, and the rest of Europe accounted for 53% of global clinical trial starts. As of 2023, this figure stood at 33%.
- During this period, Asia, and China in particular, has significantly grown its share of global clinical trial starts, with China moving from 8% of trial starts in 2013, to 29% in 2023

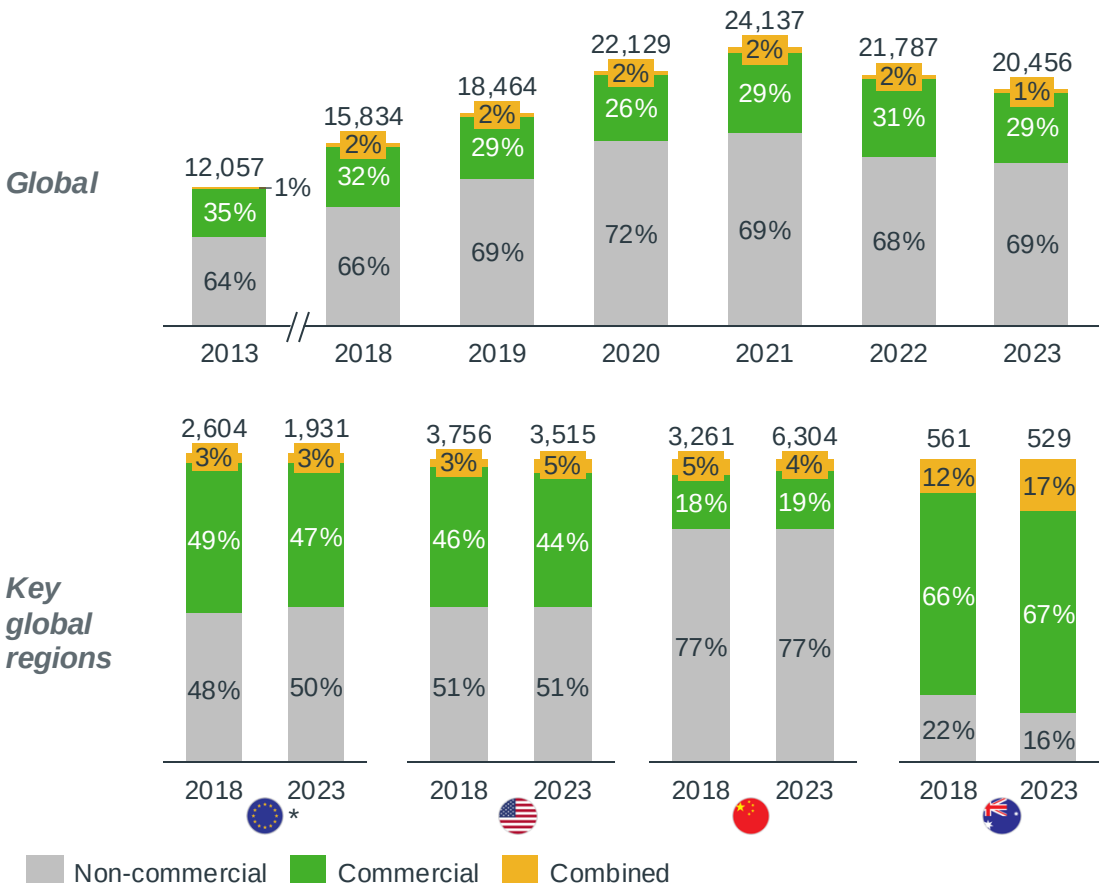
China's growth may be attributed to various factors, including National Reimbursement Drug List (NRDL) expansion, a large pool of treatment naïve patients, and an increase in China-headquartered companies sponsoring trials, especially in Phase I, oncology, and cell and gene therapy. However, China's clinical trial activity growth is primarily driven by trials conducted solely within China (single country trials).

Meanwhile, the relatively stable number of EEA trials, amidst the rising global trial numbers, has led to the EEA's share of trials decreasing from 18% in 2013, to 15% in 2018, to 9% in 2023.

Note: Medical device trials and terminated/suspended trials were excluded. ROW includes LATAM, Middle East & Africa. Rest of Europe includes Russia. Trial with sites in multiple regions were counted once for each region.
Abbreviations: CAGR: compound annual growth rate, ROW: rest of world
Source: Clinical Trial Repository (Access Date: April 30th, 2024). IQVIA Expertise; IQVIA Institute

The EEA has a broadly even split of commercial and non-commercial trials; both the EEA and US have seen a slight fall in commercial share since 2018

Number of global clinical trial starts by sponsor type (2013, 2018-2023; Phase 1-4)



Global clinical trials are predominantly sponsored by non-commercial stakeholders, with a relatively stable 70% -30% split over time, however there is significant regional variation.

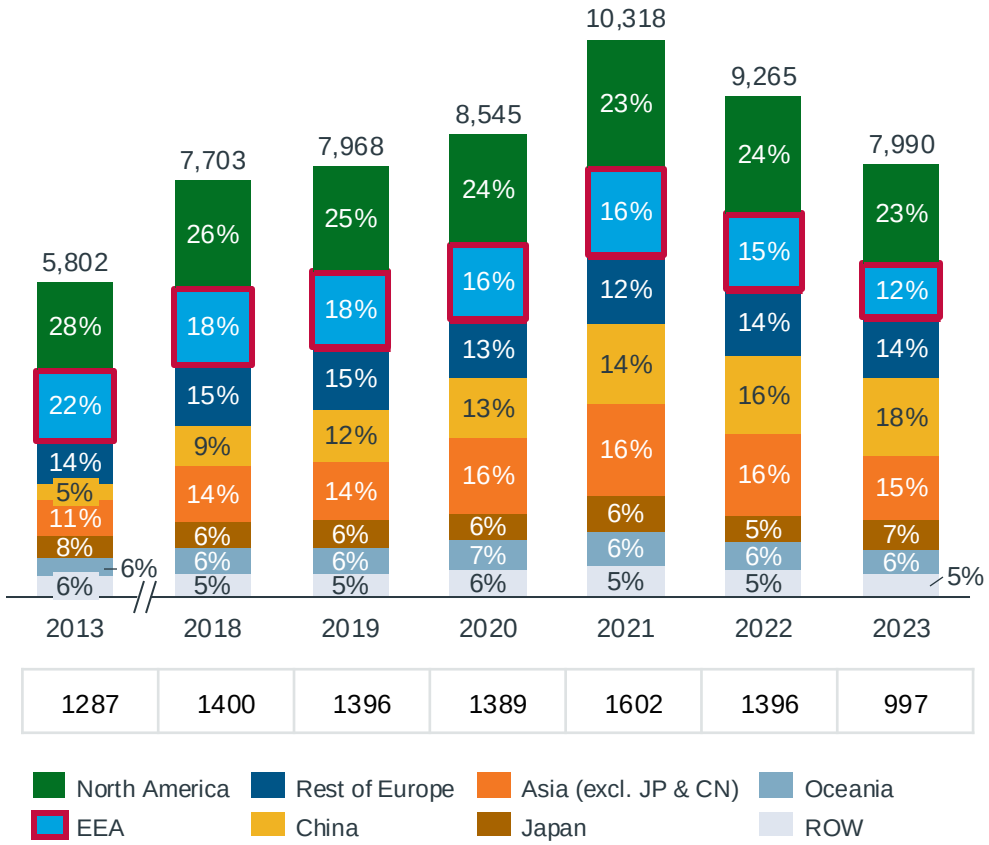
- Within EEA and the US, the split of commercial vs. non-commercial trials is broadly even, however, there has been a 2-percentage point decline in commercial share since 2018 in both regions
- In China, over three quarters (77%) of the trials have a non-commercial sponsor. This can be in part explained by China's focus on single-country trials, which are more likely to have a non-commercial sponsor
- In Australia, the opposite is true, where commercial trials constitute the majority. Industry reports suggest Australia is viewed as an attractive location for clinical trials, due to its medical & research expertise, dedicated infrastructure (particularly for Ph1 trials) and a streamlined regulatory and ethics approval process, and benefitting from geographic proximity to Asia

*Commercial share within individual member states varies between ≈30-60%. European level commercial value (49%, 47%) counts multi-country EEA trials once, to allow comparison to comparator countries

Note: Combined sponsors: any trials with more than one type of sponsor (non-commercial, EBPs, mid pharma, large pharma); Medical device trials and terminated/suspended trials were excluded.
Source: Clinical Trial Repository (Access Date: April 30th 2024); MTPConnect. (2021). Australia's Clinical Trials Sector; IQVIA Expertise; IQVIA Institute

EEA clinical trial starts were broadly stable in 2018-2022, and fell in 2023; this represents a fall in global share from 18% to 12% between 2018-2023

Number of global commercial clinical trial starts by region (2013, 2018-2023; Phase 1-4)



Top countries holding the highest number of commercial trials (2018-2023, Phase 1-4)

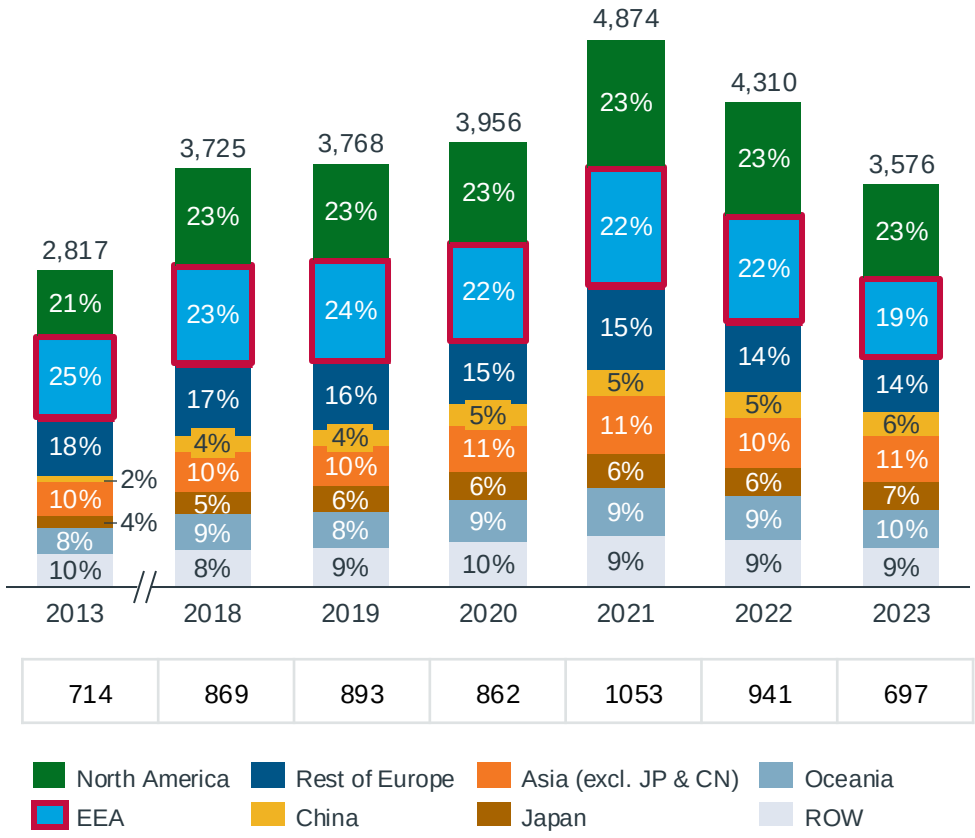
Country	2018	2023	CAGR
US	1850	**1719**	-2%
China	727	**1412**	14%
Japan	472	**546**	3%
Spain	491	**485**	0%
South Korea	491	**444**	-2%
Australia	436	**444**	0%
UK	566	**437**	-5%
Canada	473	**429**	-2%
Germany	618	**417**	-8%

- The number of commercial clinical trial starts has increased by 38% over the last decade. Meanwhile, EEA's share of total commercial trials declined from 22% (2013), to 18% (2018), to 12% (2023)
- This performance has been driven by two key trends:
  - A flat-lining or decline in absolute trial starts, in many EEA countries
  - Significant growth in absolute trial starts in China, Japan, and other non-Western markets
- The US remains the largest single country for commercial clinical trial starts; with China rapidly closing the gap
- However, underlying these trends is an increase in the number of single country commercial trials in the US and China. Europe's fall in global share is significantly less pronounced when considering *multi-country* commercial trials only (see slide 16),

Note: Medical device trials and terminated/suspended trials were excluded. ROW includes LATAM, Middle East & Africa. Rest of Europe includes Russia. Trial with sites in multiple regions were counted once for each region.
Abbreviations: CAGR: compound annual growth rate, ROW: rest of world
Source: Clinical Trial Repository (Access Date: April 30th, 2024).

Considering commercial *multi-country* trials, EEA performs relatively strongly, though has seen a small decline in global share from 23% to 19%, since 2018

Number of global commercial multi-country clinical trial starts by region (2013, 2018-2023; Phase 1-4)



When considering only multi-country commercial trials, the EEA performs strongly in the global context, though has lost share in recent years:

- EEA's share of commercial multi-country trials (MCT) trials declined from 25% (2013), to 23% (2018) to 19% (2023), behind only North America

Compared to single-country trials, MCTs require greater coordinated activity with multiple health authorities, and management of different country timeframes for regulatory review and approval. However, MCTs can enable faster, more diverse recruitment, and accelerated multi-country regulatory submission

EEA's activity in 2023 fell below its long-term average, which corresponds with several factors:

- Increasing clinical trial capabilities in non-EEA countries, particularly in Oceania and Asia
- EU Clinical Trial Regulation (EU CTR) entering force (1 Jan 2023) and IVDR (enters force 2022) and Medical Device Regulation (26 May 2021)
- Post-pandemic impact on healthcare systems and economies

China (and Asia more widely) represent a smaller share of global MCTs, given the large proportion of trials in China that are single-country focused.

Note: Medical device trials and terminated/suspended trials were excluded. ROW includes LATAM, Middle East & Africa. Rest of Europe includes Russia. Trial with sites in multiple regions were counted once for each region.
Abbreviations: CAGR: compound annual growth rate, ROW: rest of world
Source: Clinical Trial Repository (Access Date: April 30th, 2024).

EEA has a relatively high share of Phase 2 & 3 trials, which are important for patients; however, the decline in Phase 1, may limit future trial opportunities

Number of global commercial clinical trial starts by phase (2013, 2018-2023; Phase 1-4)

Global commercial growth has mainly been fueled by the rise in Phase 1 trials, which have seen a 4.5% growth (2018-2023 CAGR), higher compared to overall 4% growth of commercial clinical trials

In the EEA, the trend contrasts with the global picture, as most trials are in Phase 2 and 3, with a slight decrease in Phase 1 trials in 2023.

Whilst Phase 2 and 3 trials are particularly important for patients, a reduction in Phase 1 trials may lead to a reduced 'pipeline' of future trials, particularly in areas where specialized knowledge or equipment is required to deliver the investigational therapy, which may be established during Phase 1.

Analysis from IQVIA Institute suggests EEA has seen relative or absolute decline in most categories of trials, such as:

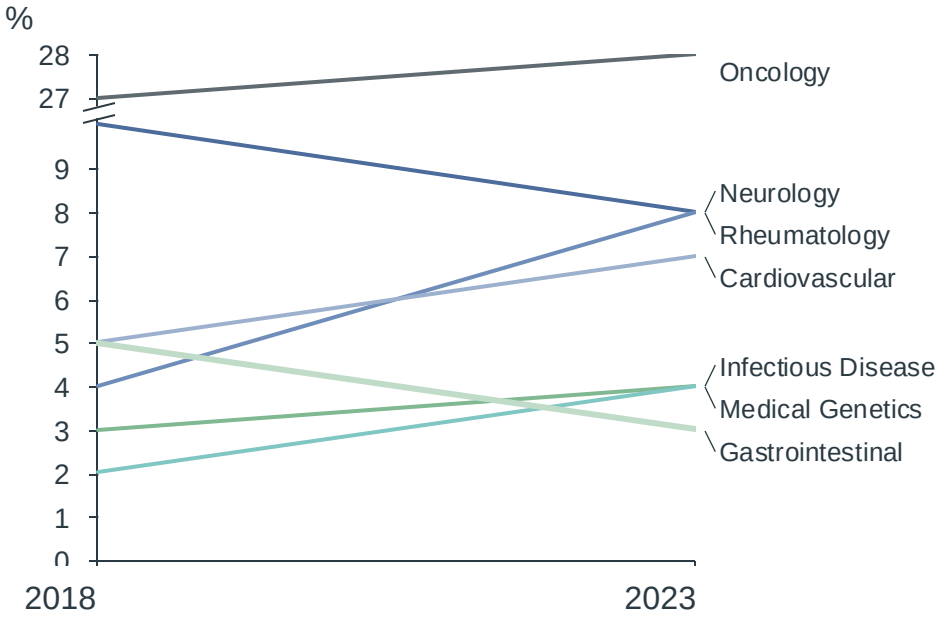
- Phase 1 oncology and Phase 2/3 oncology
- Cell and Gene Therapy (CaGT)
- Biosimilars
- Rare diseases

Conversely, China has grown its global share, particularly through an increase in Phase 1 oncology, Phase 2/3 oncology, and cell and gene therapy trials

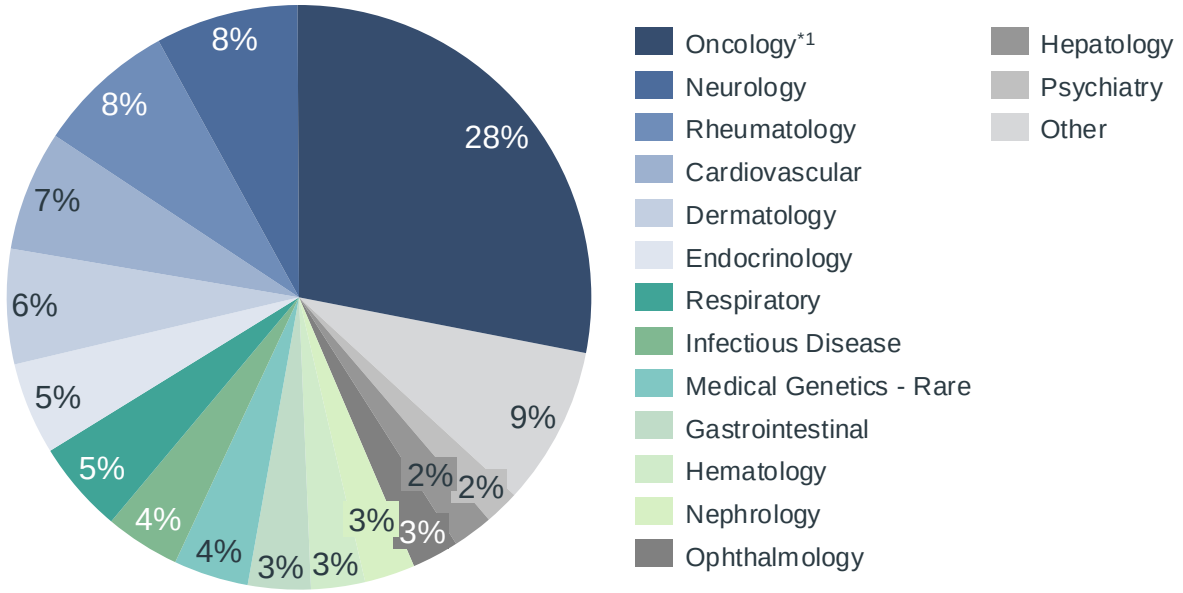
Note: Phase 2 includes Phase 1/2, 2a & 2b trials, Phase 3 includes Phase 2/3. Medical device trials and terminated/suspended trials were excluded. Trial with sites in multiple EEA countries were counted once within EEA
Abbreviations: CAGR: compound annual growth rate
Source: Clinical Trial Repository (Access Date: April 30th 2024)

Within EEA commercial trials, oncology remains the dominant therapeutic area; cardiovascular and rheumatology increased share, whilst neurology fell

Share of commercial clinical trials by therapy area, within EEA (Phase 1-4, 2018-2023)



Share of commercial clinical trials by therapy area (Phase 1-4, EEA, 2023)

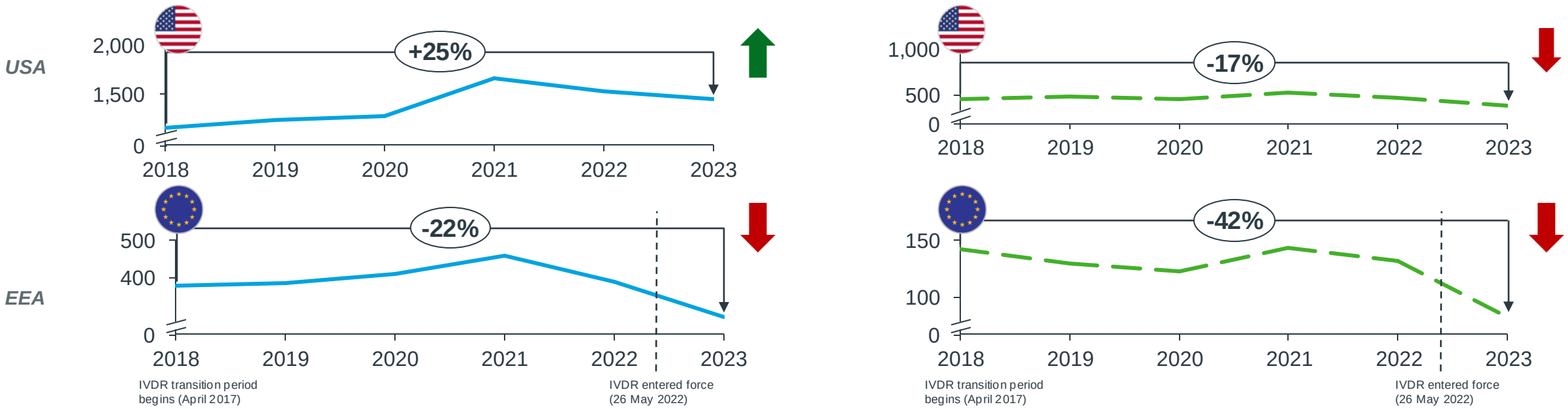


Oncology remains the largest TA for EEA trials, accounting for more than 25% of new trial starts. Neurology is the second largest TA, though has seen a fall in activity in recent years. These trends broadly reflect the global TA picture. Infectious-disease trials are slightly lower than global average, and rheumatology higher than the global average. Recent EEA share growth is seen in cardiovascular, rheumatology and infectious diseases, at the expense of neurology and gastrointestinal trials.

Note: Phase 1-4 commercial trials considered. Medical device trials and terminated/suspended trials were excluded. Trial with multiple therapy areas are counted once per therapy area.
*1 Oncology includes haematology-oncology treatments; *2 The rank is based on the absolute number and the share of the given year. Abbreviations: TA: therapy area, CV: cardiovascular
Source: Clinical Trial Repository (Access Date: April 30th 2024)

In oncology and neurology, the EEA has experienced contrasting trends to US; IVD regulation, among other factors, may have influenced trial decisions

Total number of commercial oncology and neurology trial starts in 2018-2023; Phase 1-4



In the EEA, despite the 'Beating Cancer Plan', oncology trial starts have fallen consistently since 2021, and are now below 2018 levels. This contrasts to the US, which saw an increase in 2021, and levels have been maintained. The fall in EEA may be driven by several factors. In the EU, the in-vitro diagnostic regulation (IVDR) transition period began in 2017, which introduced more stringent requirements for the designation of Notified Bodies, with increased control and monitoring by the national competent authorities and EU Commission. This regulation affects clinical trials using in-vitro diagnostics (e.g., for patient selection, allocation and monitoring), which is particularly relevant to oncology trials, though can affect many TAs.

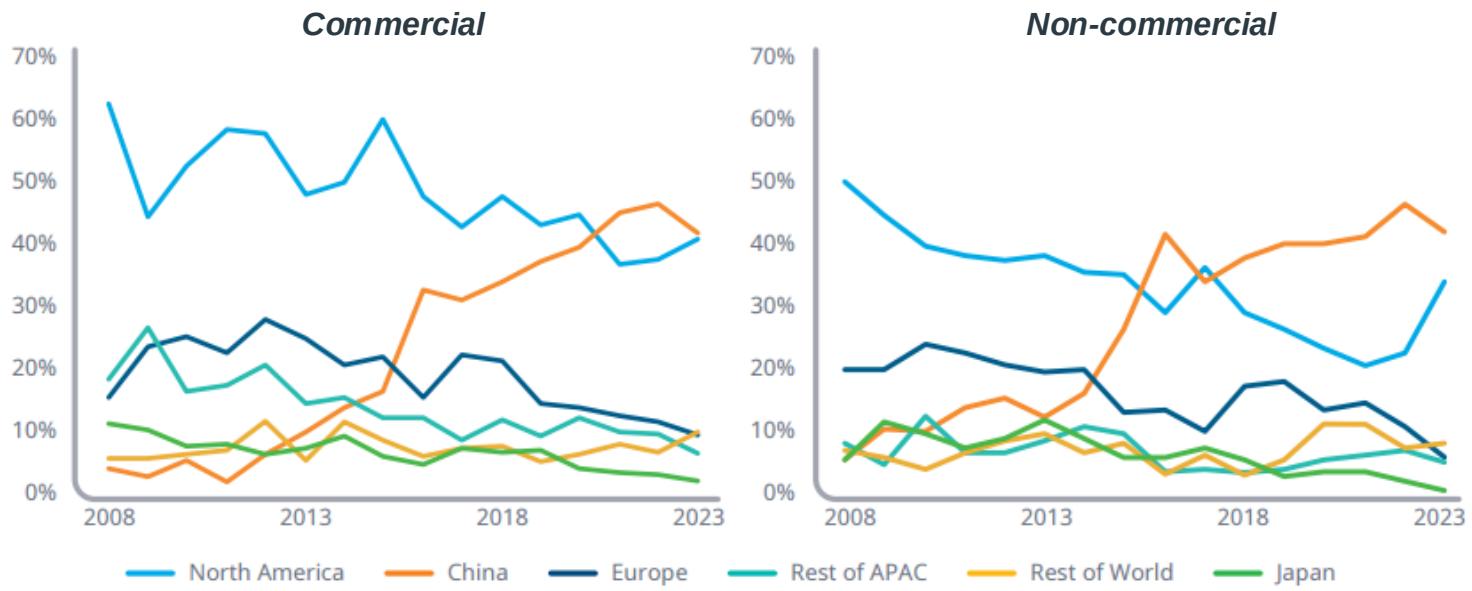
A fall in new starts in neurology in the EEA may be driven by a combination of local policy factors (including IVDR), but also broader industry trends (reduced biopharma R&D investment in 2022, recent R&D challenges in neurology).

Note: Phase 1-4 commercial trials considered. Medical device trials and terminated/suspended trials were excluded. Trial with sites in multiple EEA countries were counted once within EEA.
Abbreviations: TA: therapy area, IVDR: In Vitro Diagnostic Regulation
Source: Clinical Trial Repository (Access Date: April 30th 2024)| EU Beating Cancer Plan

Europe's share of Cell and Gene Therapy trials has decreased since 2013, whilst China has experienced rapid growth in the last decade

Cell and Gene Therapy (CaGT) spotlight

Share of cell and gene therapy trial starts by geography (2013-2023)



Europe's participation in global cell and gene therapy trials has steadily decreased since 2013.

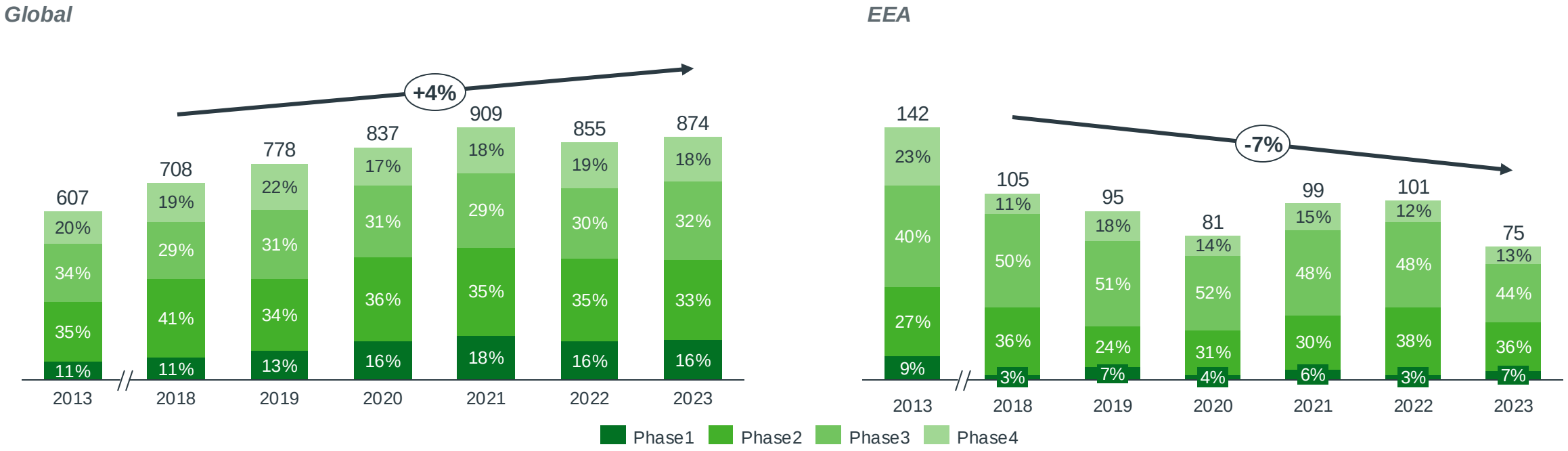
During this period, China has seen a dramatic rise in CaGT trials since 2013, to become the leading region. This trend may be attributed to a favourable regulatory environment, funding streams, and strategic focus on these technologies

Between 2014-2022, The US share of CaGT trials declined, though the US remains the second-largest region for commercial and non-commercial trials. Since 2021, there has been a notable increase in non-commercial CaGT trials in the US, suggesting the US is increasing its focus in this area

Note: ATMP: Advanced Therapy Medicinal Products
Abbreviations: ATMP: advanced therapy medicinal product, CaGT: cell and gene therapy
Source: Strengthening Pathways for Cell and Gene Therapies, IQVIA Institute

The number of paediatric trials are declining in the EEA, against a backdrop of global limited growth

Number of paediatric clinical trial starts by phase (2013, 2018-2023, Phase 1-4)

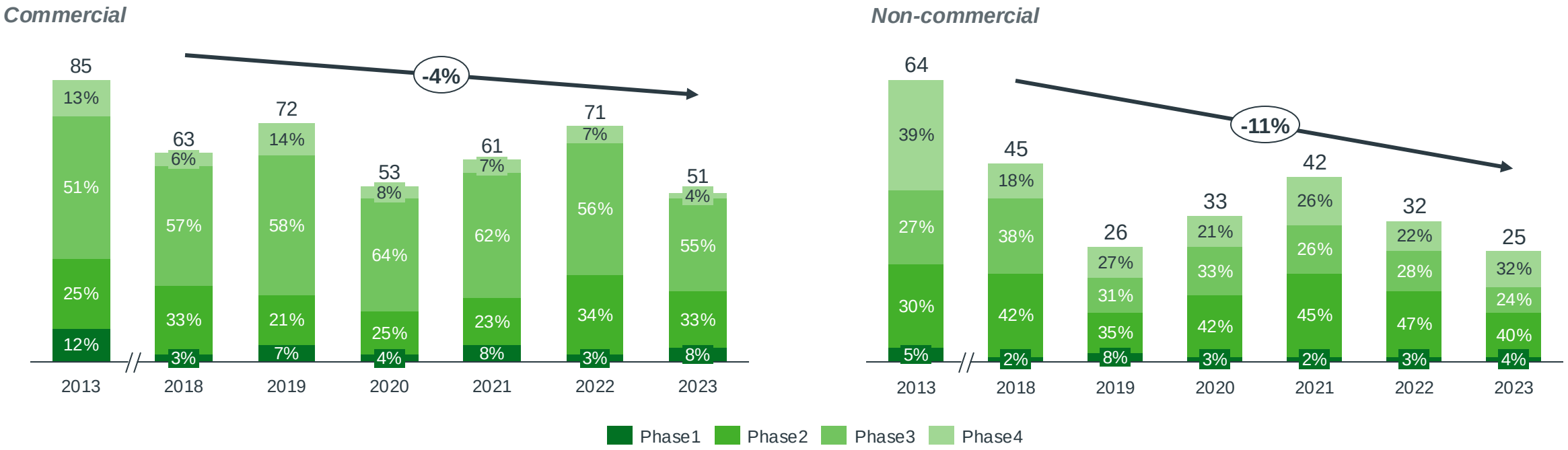


Globally, there has been a small increase in paediatric clinical trials across phases, with this trend primarily driven by China and other non-Western markets. Conversely, in the EEA, despite a small rise in COVID related trials during 2021-22, there has been a decline across phases since 2013

Note: Phase 2 includes Phase 1/2, 2a & 2b trials, Phase 3 includes Phase 2/3. Medical device trials and terminated/suspended trials were excluded.
Source: Clinical Trial Repository (Access Date: June 12th 2024)

Within the EEA, there has been a decline in both commercial and non-commercial paediatric sponsored trials, suggesting systemic challenges

Number of EEA paediatric clinical trial starts by phase (2013, 2018-2023, Phase 1-4)



In the EEA, both commercial and non-commercial paediatric disease clinical trials declined over last 6 years, with commercial trials falling by 4% and non-commercial trials seeing a steeper decline (11% reduction). A decline in paediatric research has been highlighted by Evelina London Children's Hospital, which showed:

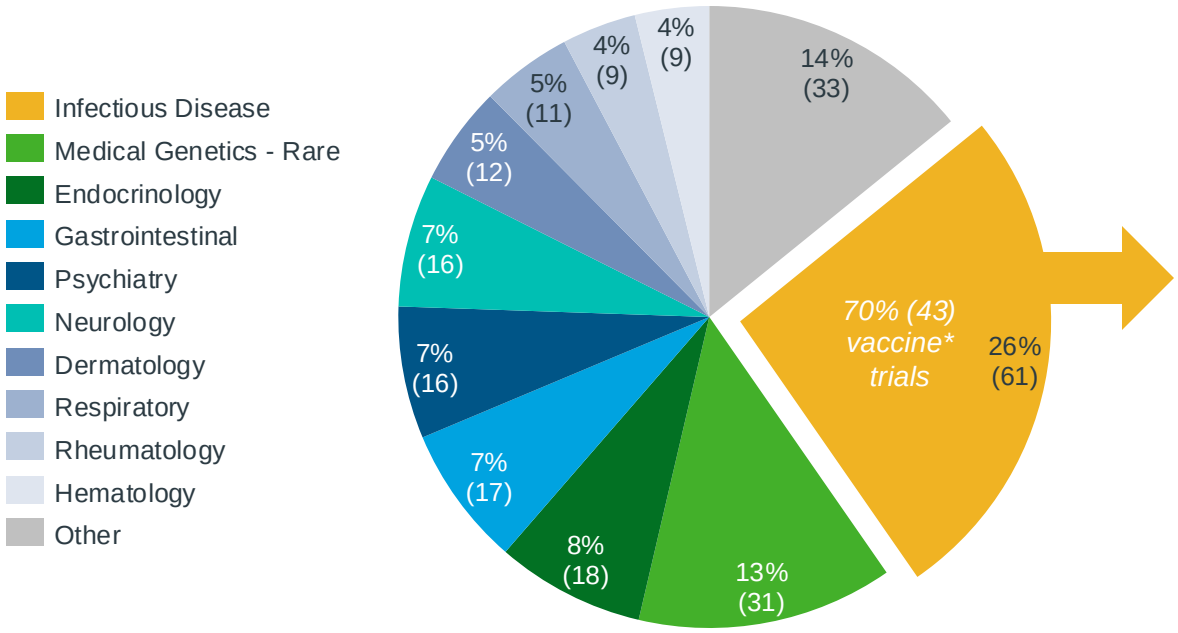
- 30% reduction in research outputs for child health compared to pre-pandemic level, with the number of paediatric clinical trials published falling each year at an increasing rate.
- Similar trends in Europe and US, across all childhood conditions except respiratory diseases, with Europe and the UK having the greatest reductions globally

Note: Phase 2 includes Phase 1/2, 2a & 2b trials, Phase 3 includes Phase 2/3. Medical device trials and terminated/suspended trials were excluded.
Source: Clinical Trial Repository (Access Date: April 30th 2024)

Most commercial paediatric trials are focused on infectious diseases and rare diseases; 'paediatric-only' oncology trials are relatively limited

Paediatrics Spotlight

Global commercial paediatric trial starts in 2023 (Phases 1-4, top 10 TAs, n=214)



Commercial paediatric infectious disease vaccine trial starts in 2023*

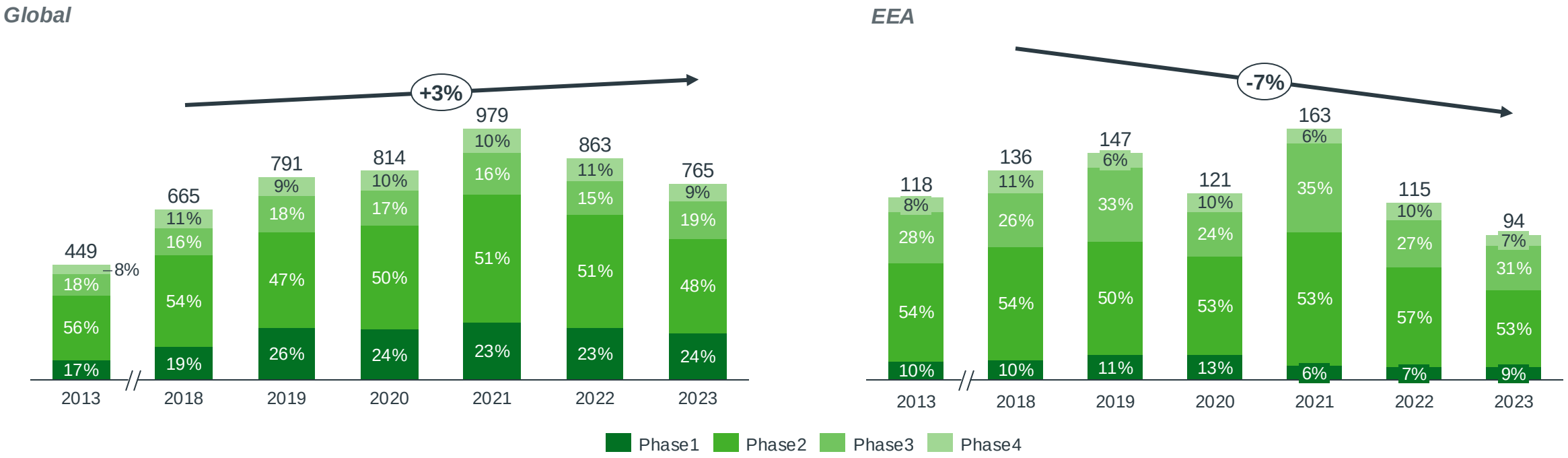
Country	#trials	%share
CN	13	23%
JP	7	12%
US	6	11%
ZA	3	5%
IN	3	5%
PH	2	4%
PL	2	4%
ES	2	4%
ID	2	4%

North America	South America	Europe
Asia	Oceania	Africa

Note: Medical device trials and terminated/suspended trials were excluded. Trial with multiple therapy areas are counted once per therapy area.
*Trial with sites in multiple countries were counted once per country. Abbreviations: TA: therapy area
Source: Clinical Trial Repository (Access Date: April 30th 2024)

In rare diseases, trial starts in the EEA are declining, whereas globally, trial starts remained broadly flat in 2023 compared to 2019

Number of rare diseases clinical trial starts by phase (2013, 2018-2023, Phase 1-4)

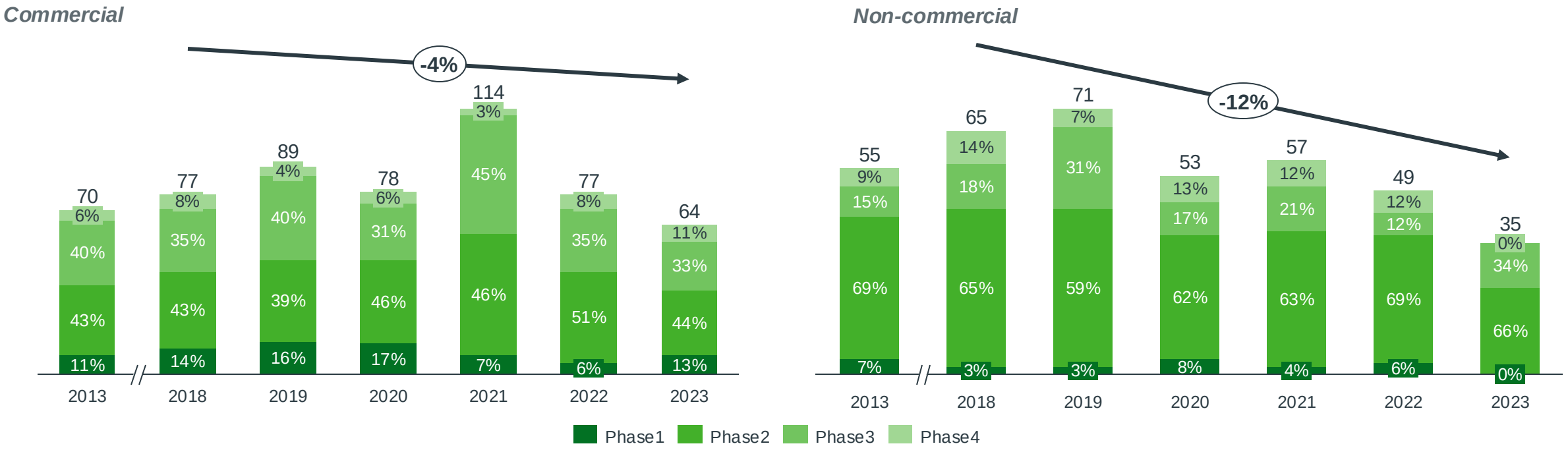


Globally, despite an uptick in 2021, rare disease clinical trials are also relatively flat, with 2023 showing fewer trial starts than 2019. EEA has seen a more notable decline, with 20% fewer trial stars in 2023 vs 2018. The fall is primarily driven by a reduction in Phase 1 and Phase 3 trials. Given the particular importance of emerging biopharma to rare disease trials, the global and European trends may be influenced by changes in availability of venture capital funding. However, a causal link has not been explored in this report.

Note: Phase 2 includes Phase 1/2, 2a & 2b trials, Phase 3 includes Phase 2/3. Medical device trials and terminated/suspended trials were excluded.
Source: Clinical Trial Repository (Access Date: June 12th 2024)

EEA rare disease trials are primarily driven by commercial sponsors, with a significant decline in non-commercial rare disease activity in 2023

Number of EEA rare disease clinical trial starts by phase (2013, 2018-2023, Phase 1-4)

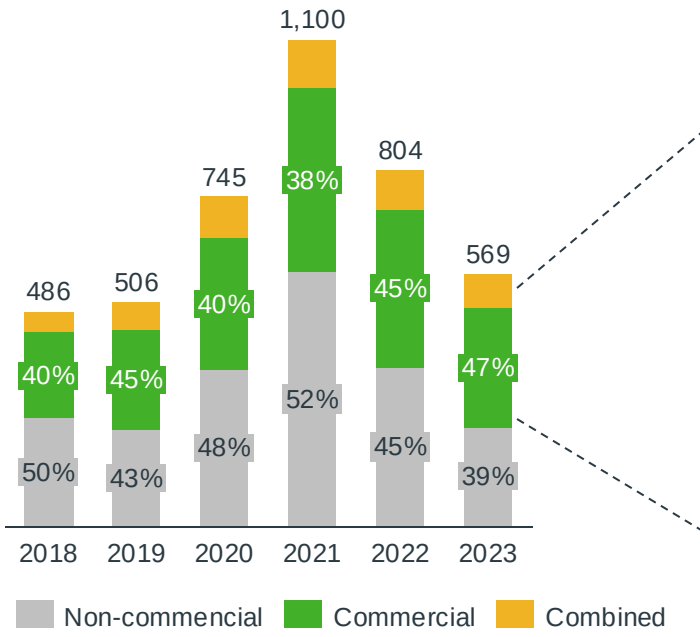


Within the EEA, both commercial and non-commercial rare disease trials declined over last 6 years, with non-commercial trials seeing a steeper decline than commercial trials, suggesting systemic challenges are influencing the rare disease trial ecosystem

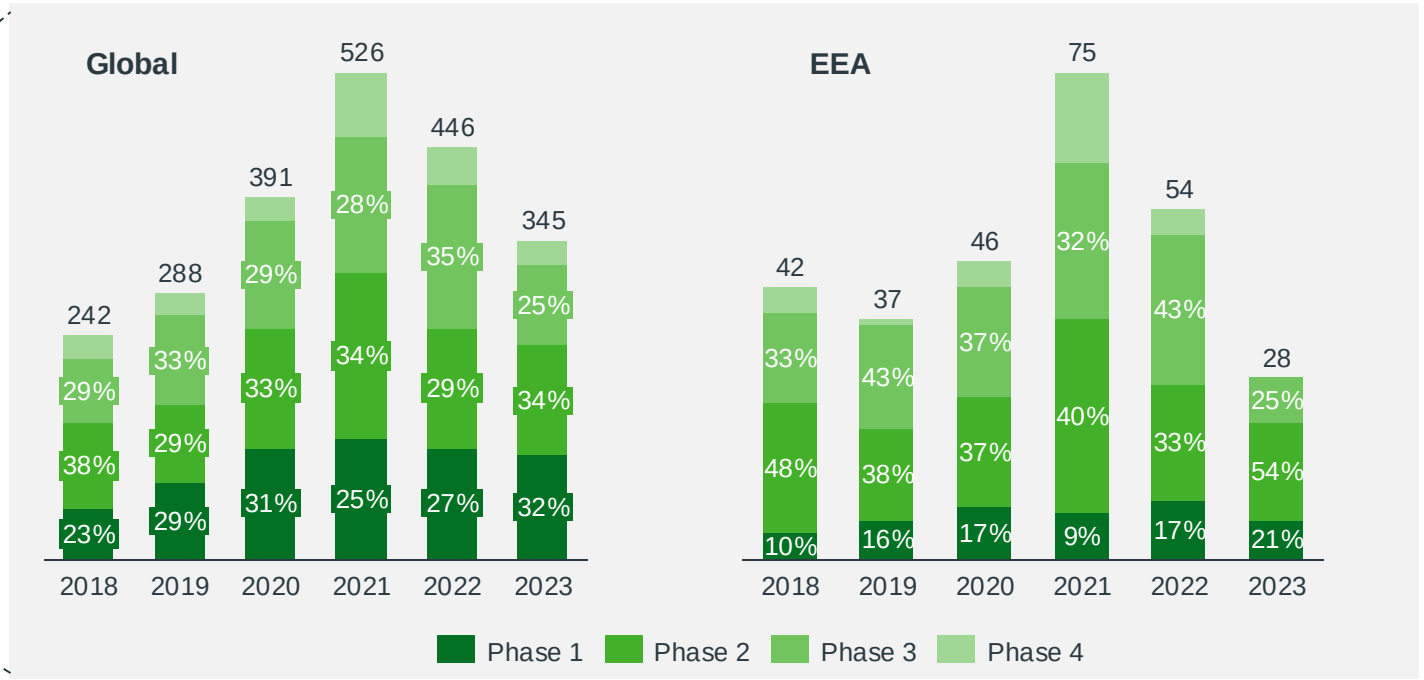
Note: Phase 2 includes Phase 1/2, 2a & 2b trials, Phase 3 includes Phase 2/3. Medical device trials and terminated/suspended trials were excluded.
Source: Clinical Trial Repository (Access Date: June 12th 2024)

Within the immunisation field, global and EEA trial starts have fallen back from a COVID peak; EEA has seen a notably large fall in Phase 3 trials

Number of global immunisation trial starts by sponsor type (2018-2023, Phase 1-4)



Number of commercial immunisation trial starts by phase (2018-2023, Phase 1-4)



The total number of immunisation clinical trial starts in 2023 has fallen back to pre-COVID levels, after major boost during 2020, 2021 and 2022 due to COVID-related research. As of 2023, commercial sponsors now account for more than 50% of new starts, having increased in absolute terms, driven my increased activity in China

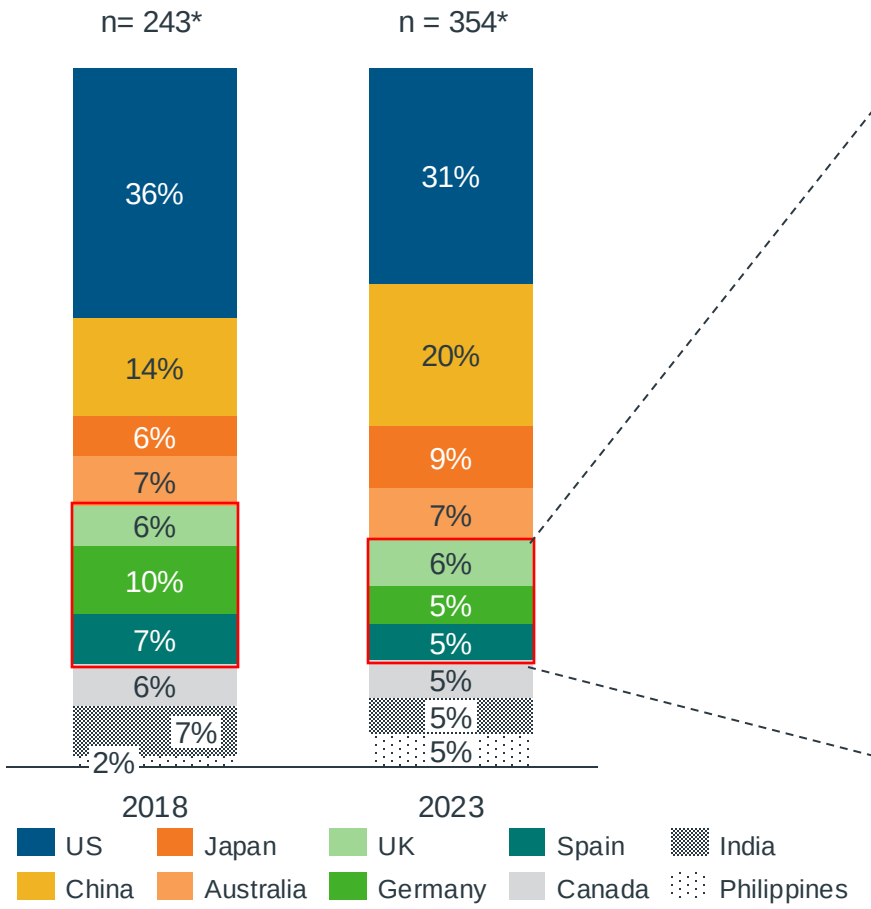
Globally commercial immunisation trials growth has been driven by an increase in Phase 1 trials (+103% new starts in 2023 vs. 2018). However, EEA has seen a fall in commercial trials (-33% new starts in 2023 vs 2018). This represents a decline in global share from 17% in 2018 to 8% in 2023

EEA's fall has been driven by a decrease in the number of Phase 3 immunisation trials, whilst Phase 1 has remained stable. Phase 4 EEA immunisation trials have also fallen sharply. The trends in Phase 3 and Phase 4 should be monitored to confirm if this continues in future years

Source: Clinical Trial Repository (Access Date: April 30th 2024)

Geographically, EEA has lost immunisation trial starts to Asia, Oceania and potentially the UK; Belgium and Finland have seen a particularly large fall

Number of global commercial immunisation trial starts for Top 10 countries (2018-2023, Phase 1-4)



Number of commercial immunisation trial starts for Top 10 EEA countries (2018-2023, Phase 1-4)

2018	2023	CAGR
24	**19**	-4%
17	**19**	2%
14	**12**	-3%
8	**8**	0%
14	**8**	-9%
7	**7**	0%
2	**6**	20%
6	**5**	-3%
7	**4**	-9%
11	**3**	-19%
3	**3**	0%
14	**23**	9%

Caution required when interpreting these trends, given the small numbers of trials

Globally, there has been a relative shift in immunisation trials away from US and EEA towards China, Japan and Australia

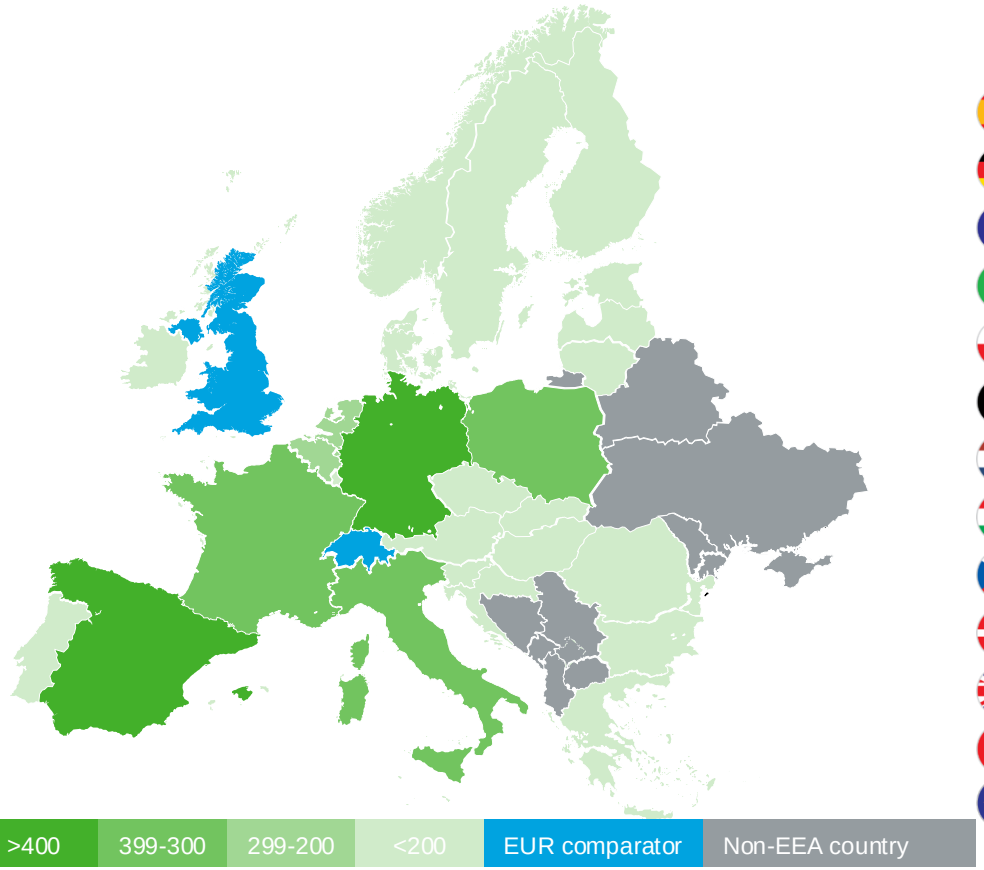
Within EEA, most countries have seen a fall in trial starts, with Finland, Norway, Belgium, and to a lesser extent, Germany and France seeing a drop. Denmark and Spain have seen growth, and outside the EEA, UK has seen a particular increase

Belgium has historically led in per-capita immunisation trials in EEA, however stakeholders in Belgium[1] have raised concerns that post-CTR, the timelines for regulatory and ethical approval have significantly increased and consultation of a principal/coordinating investigator (PI) by Ethics Committees is no longer common practice.

Source: Clinical Trial Repository (Access Date: April 30th 2024); (1) *Does not sum to total commercial immunisation trials when counted by phase, as each country is counted individually in this chart

Across all commercial trials in the EEA, there is variation in country-level performance; Spain recently overtook Germany in clinical trial starts

Number of EEA commercial clinical trial starts in 2018 and 2023, top 10 countries



2018	2023	CAGR
491	**485**	-0.2%
618	**417**	-7.6%
439	**389**	-2.4%
378	**343**	-1.9%
332	**300**	-2.0%
305	**218**	-6.5%
282	**210**	-5.7%
205	**161**	-4.7%
199	**147**	-5.9%
156	**118**	-5.4%
573	**439**	-5.0%
120	**107**	-2.3%
1253	**920**	-6.0%

All but three EEA countries* saw a fall in the absolute number of trial starts in 2023 vs 2018

Spain, Germany, France and Italy remain the largest countries for clinical trial activity within the EEA

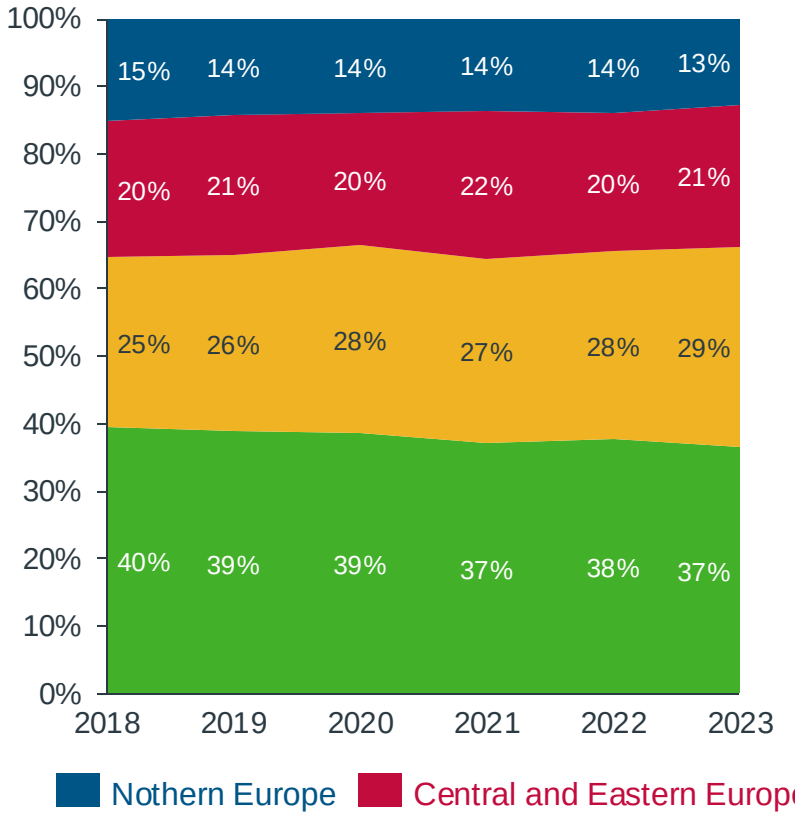
- In Spain, over the past decade, investment in clinical trials has risen at an average annual rate of 5.3%, climbing from EUR 470 million in 2011 to nearly EUR 800 million in 2021. Factors attracting investment may include quality of Spain's healthcare system, successful implementation of new European legislation on clinical trials, and an effective commercial/ non-commercial clinical trial collaboration model
- The recent decline in German trials is attributed, in part, to extensive negotiation times between companies and research institutions, and highly stringent data protection laws, which may slow patient recruitment efforts

*Slovakia, Portugal and Greece

Note: Limited data coverage on Lichtenstein, Malta and Iceland; Phase 1-4 commercial trials considered. Medical device trials and terminated/suspended trials were excluded. *[1] 2018-2023 CAGR
Source: Clinical Trial Repository (Access Date: April 30th 2024); Farmaindustria, TaylorWessing

Combined, there has been a shift in trial activity towards Southern Europe, though Denmark and Belgium remain high on a per capita basis

Proportion of EEA commercial clinical trial starts by sub-region, 2018-2023



Commercial clinical trials in EEA countries per capita (100 000) in 2023

	Country	#trials per capita
1	Denmark	2.00
2	Belgium	1.84
3	Bulgaria	1.72
4	Estonia	1.71
5	Hungary	1.68
6	Latvia	1.58
7	Czech Republic	1.35
8	Slovakia	1.28
9	Austria	1.22
10	Netherlands	1.17
	UK	0.64
	Switzerland	1.22
	US	0.51

Considering the distribution of EEA trials by sub-region, Western Europe has declined by 3 percentage points since 2018, driven by a steep decline in trial starts in Germany and Belgium, and a small decline in France.

Southern Europe has experienced a 4-percentage point increase, predominantly driven by the performance of Spain, which has attracted an increasing proportion of EEA trials across an array of TAs

Central and Eastern Europe retained a constant share of EEA trials, with Poland a top 5 EEA contributor, although CEE region has seen a particular shift away from Ph2/3 primary care-focused trials

Northern Europe (Sweden, Norway, Finland) saw a small but consistent decline since 2018

On a per capita basis, smaller countries perform strongly, with Denmark and Belgium retaining the highest level of trial starts per capita in EEA

Note: Phase 1-4 commercial trials considered. Medical device trials and terminated/suspended trials were excluded. Trial with sites in multiple EEA regions were counted once per each region.
Source: Clinical Trial Repository (Access Date: April 30th 2024; IQVIA Institute (Rethinking Clinical Trial Country Prioritization)

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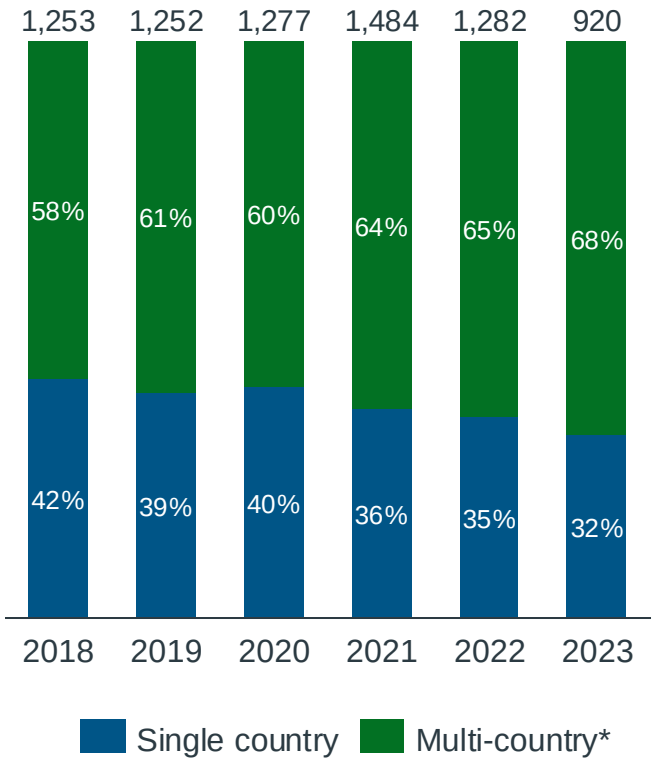
An increasing number of EEA trials are delivered in multiple countries, contrasting a recent global shift towards more single-country trials

Share of single- vs. multi-country* commercial trials started in EEA in 2018-2023



Top 10 EEA countries holding the highest number of single country commercial trials

Country	#trials	%share
France	58	20%
Germany	46	16%
Spain	35	12%
Netherlands	28	10%
Italy	26	9%
Belgium	20	7%
Sweden	14	5%
Denmark	13	4%
Poland	10	3%
Norway	8	3%

Northern Europe Central and Eastern Europe

Southern Europe Western Europe

In EEA, more than two-thirds of trials are 'multi-country' (defined as trial sites in more than one country) with this trend increasing since 2018

This finding, alongside a declining absolute number of trials, may suggest that

- There is an increasing capability to conduct trials in a range of EEA countries
- Multiple EEA countries are required to reach the desired patient population

However, other commercial and operational factors may be driving this trend

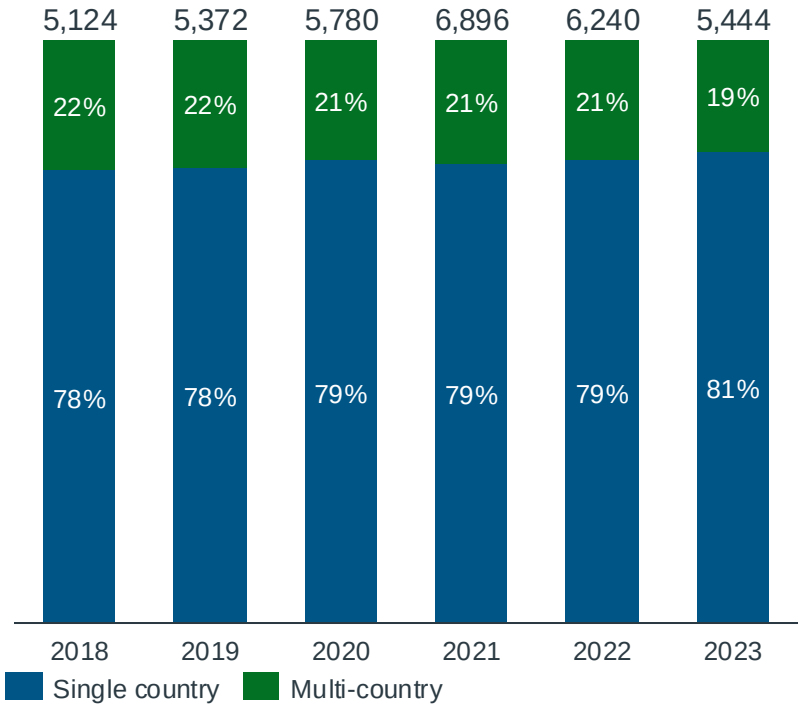
France, Germany and Spain remain the EEA countries with the greatest number of single-country trials, likely due to population size, healthcare infrastructure and research centers

Note: Phase 1-4 commercial trials considered. Medical device trials and terminated/suspended trials were excluded. Trial with sites in multiple EEA countries were counted once within EEA. *Multi-country trials defined here as involving at least one EEA country, and not excluding those with a non-EEA country as part of the trial. NB/ A similar trend is seen when restricting multi-country trials to EEA only

Source: Clinical Trial Repository (Access Date: April 30th 2024)

Globally, US, China, India and Japan are driving the rise in single-country trials

Single- vs. multi-country commercial trials, global, Phases 1-4, in 2018-2023



Single-country commercial trials initiated in 2023, Phases 1-4, top 10 countries globally

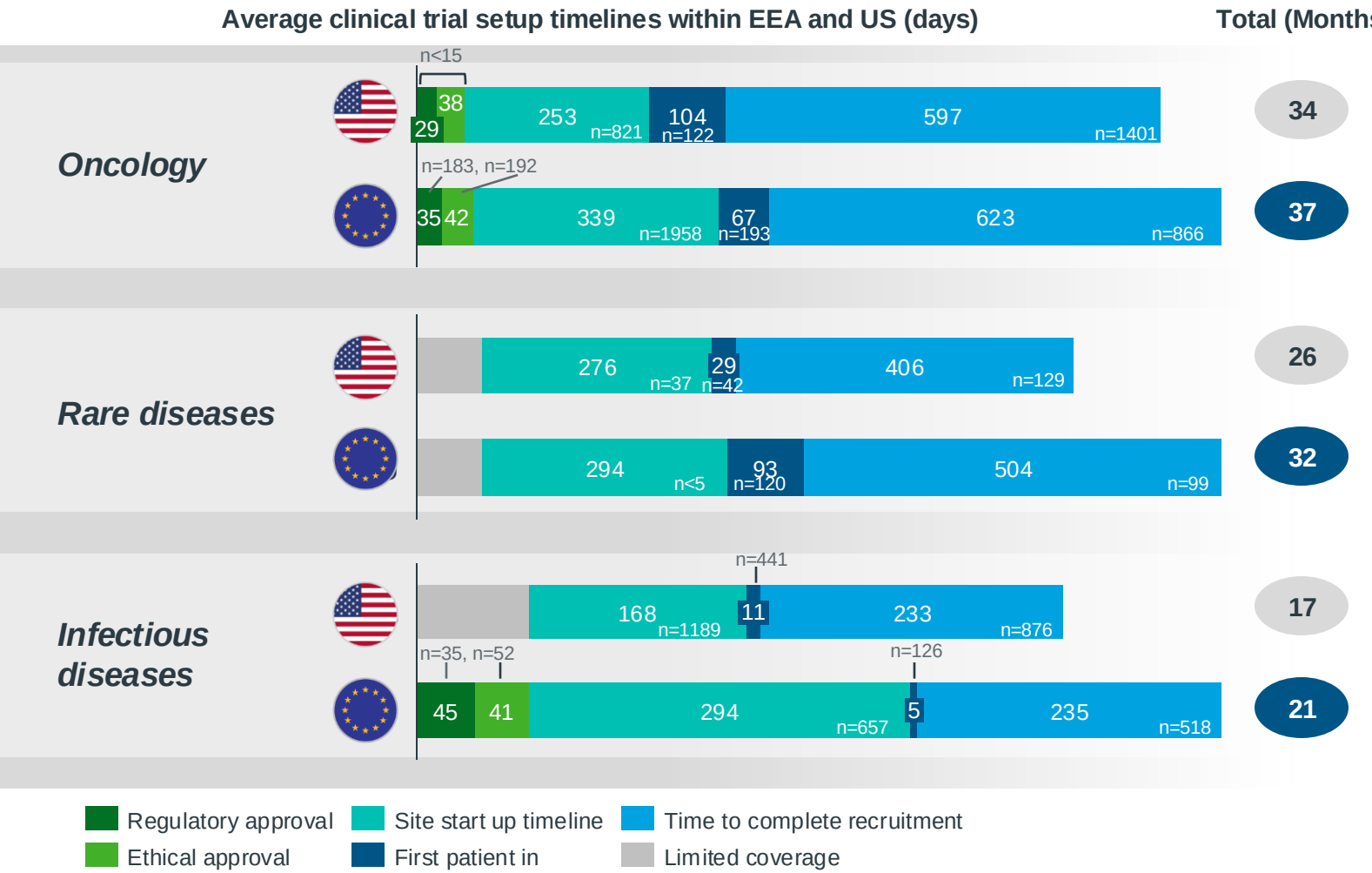
Country	#trials	%share
China	1194	27%
US	921	21%
India	321	7%
Japan	298	7%
South Korea	179	4%
Iran	131	3%
Australia	110	2%
UK	74	2%
Canada	72	2%
Thailand	71	2%

North America	South America	Europe
Asia	Oceania	Africa

- Globally, across phases, there has been an increase in the number of single-country trials, with China, US, India, Japan driving this trend
- Approximately 50% of singe-country trials are located in China and US, likely due to their large patient pool, number of local companies, regulatory requirements, and future market demand

Note: Phase 1-4 commercial trials considered. Medical device trials and terminated/suspended trials were excluded.
Source: Clinical Trial Repository (Access Date: April 30th 2024)

EEA's declining global share may be influenced by longer trial timelines; site start-up and recruitment are slower than the US, across therapy areas



Source: Clinical Trial Repository (Access Date: April 30th 2024)

Clinical trial set up timelines vary across regions and TAs. In this analysis, five steps were measured:

- Regulatory approval ; Ethical approval; Site 'start-up' Recruitment (first patient in) ; Recruitment (last patient in)

Of the five steps, site startup timeline and recruitment duration required the longest period in all three TAs explored (oncology, rare disease and infectious diseases).

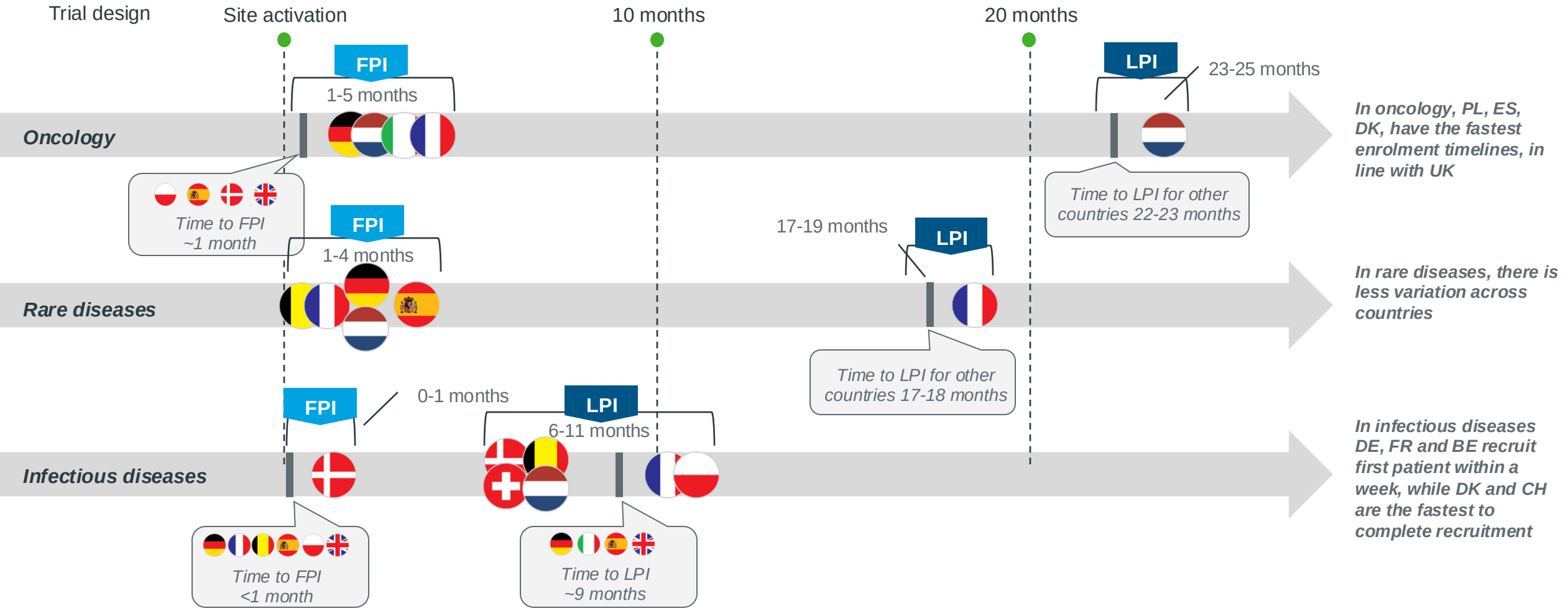
Across each therapy area, EEA timelines were longer than the equivalent US values. In infectious diseases (ID), site-start up timelines in EEA were notably longer than US. Within ID, there is variation between vaccine and non-vaccine trials. Vaccine trial start-up times were significantly longer in the US (vs. non-vaccine ID trials), but only slightly longer in the EEA

Across TAs, there is country-level variation within the EEA:

- Focusing on oncology, which represents the largest TA for clinical trials, Poland, Spain and Denmark show the fastest enrolment timelines, with a similar performance to the UK.

Within EEA, there is significant variation across countries, with Poland, Spain and Denmark showing fast recruitment rates

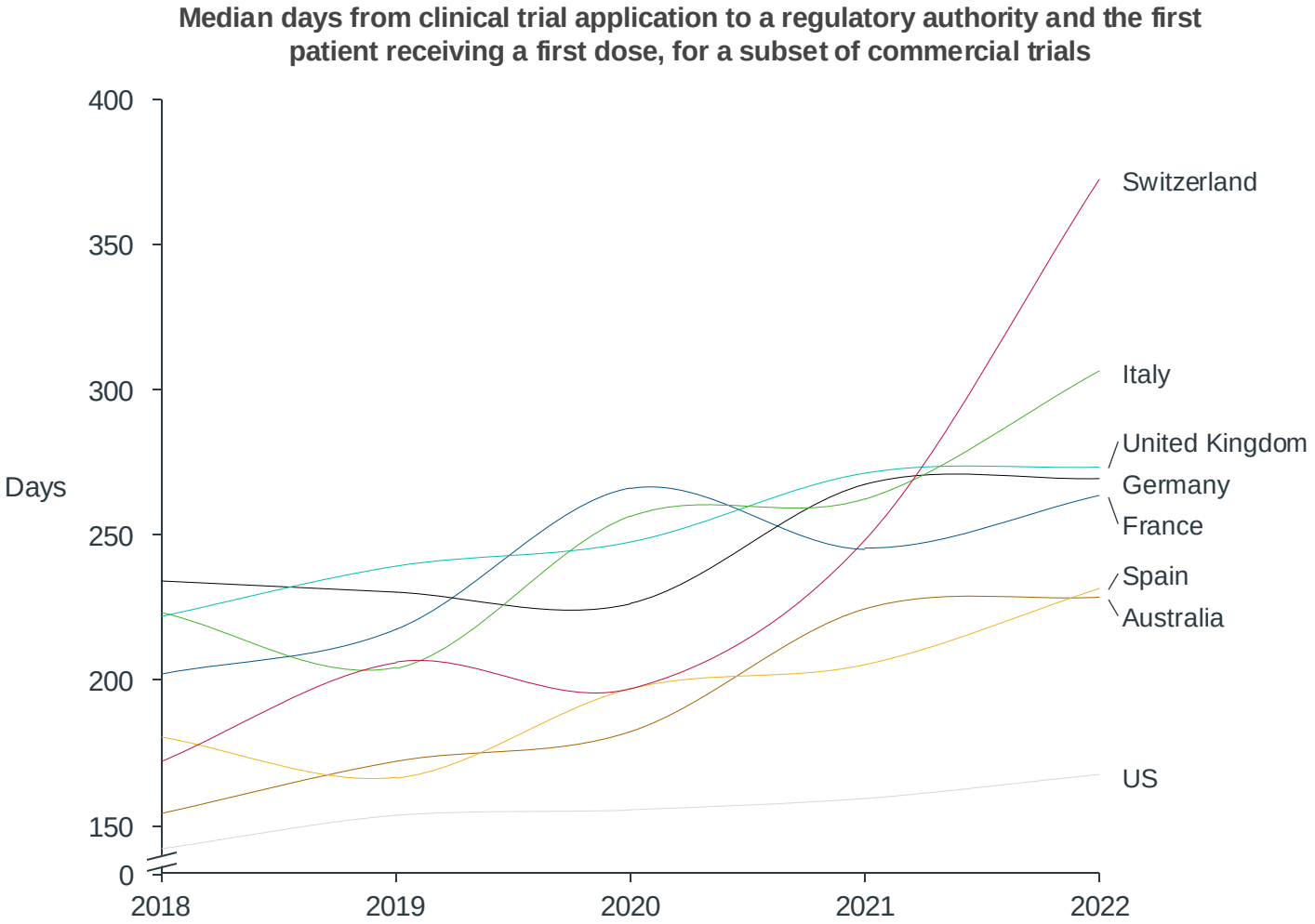
Clinical trial setup timelines within EEA and European comparator countries



Source: Clinical Trial Repository (Access Date: April 30th 2024)

FPI First patient in LPI Last patient in (recruitment completed)

However most Western countries, including the US, are seeing a slow-down in trial set-up and recruitment, potentially driven by increased trial complexity



Clinical trial set-up timeline has been increasing since 2018, in most Western markets. This may be attributed to increasingly complex trials, with a wider set of endpoints, with more granular patient recruitment requirements, and longer negotiations with hospital centers

Between 2021-22, Switzerland saw a notable significant increase in set-up timelines. As a non-EU country, Switzerland has not adopted EU's Clinical Trial Regulation, and follows local clinical trial regulations and processes

Within major EEA countries, Spain retains the shortest trial set-up timelines, though faced a 25% deceleration since 2018

Whilst also slowing, in absolute terms, US and Australia have faster timelines than most major EEA countries, with US increasing the gap to the EEA in recent years

Source: Office of Life Sciences, UK Government, 2024; ABPI

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Clinical trials are extremely valuable to patients, providing early access to medicines and the opportunity to push boundaries of scientific knowledge

Impact on patients

Clinical trials provide early access to innovative medicines

Clinical trials can provide patients with **access to innovative medicines up to 5-10 years** before commercial launch[1,2]

In some cases, clinical trials provide the only treatment option

For **rare disease patients, clinical trials play a particularly important role** in providing treatment opportunities[3]

Clinical trials allow patients to contribute to society and the future of healthcare

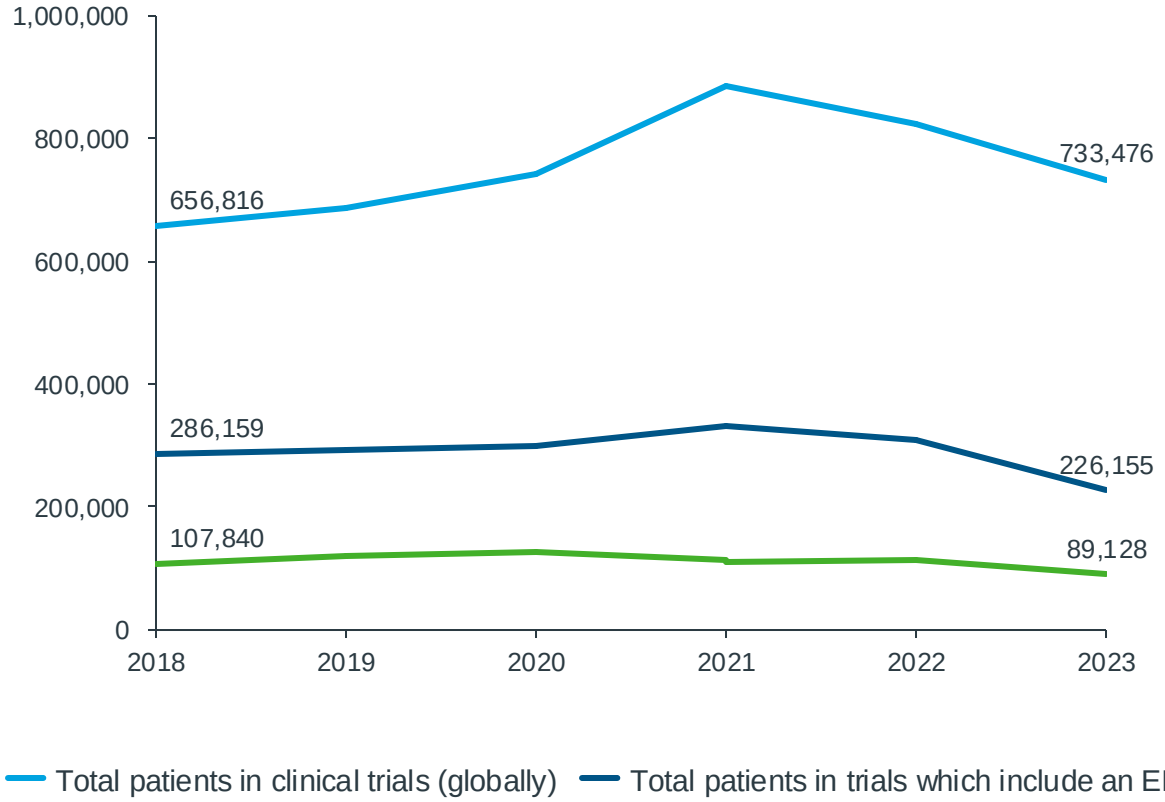
In addition to potential personal benefit, many patients take **comfort and pride in contributing medical knowledge**[2]

Source: 1. CRUK, 2. NIH 3. NORD

In recent years, the EEA has seen a decline in the number of patients enrolled into clinical trials, contrasting to global growth

Impact on patients

Total patient numbers enrolled into commercial global, EEA-only and EEA-included trials (2018-2023)



Change in patients 2018 vs.2023

70,000 more patients in clinical trials globally

60,000 fewer patients in trials involving an EEA country

20,000 fewer patients in EEA-only trials

Between 2018 and 2023, global enrollment of patients into commercial clinical trials increased by 12%, despite falling back from the major boost seen during the COVID pandemic

Conversely, in the EEA, there has been a decline in the number of patients enrolled in 'EEA-only' trials (-20%) and 'EEA-included trials' (-22%)

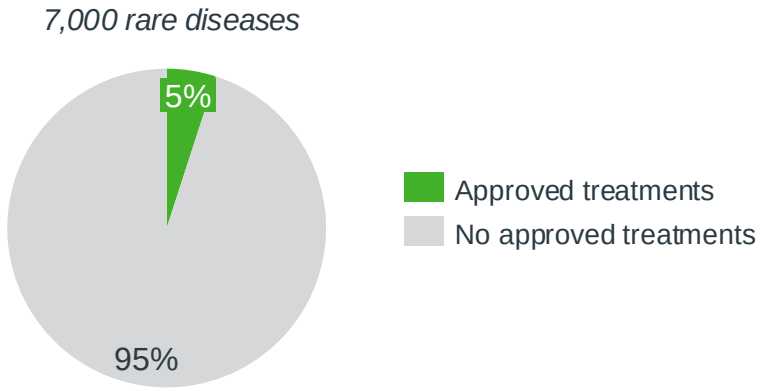
These trends follow a similar pattern to clinical trial starts, confirming that the fall in trials has not been compensated by 'larger' trials with greater number of enrolled patients

Note: Phase 1-4 commercial trials considered. Medical device trials and terminated/suspended trials were excluded.
Source: Clinical Trial Repository (Access Date: April 30th 2024)

For patients with rare diseases, a decline in patient numbers is particularly concerning, given the critical role trials play in providing treatment options

Impact on patients - Rare Disease Spotlight

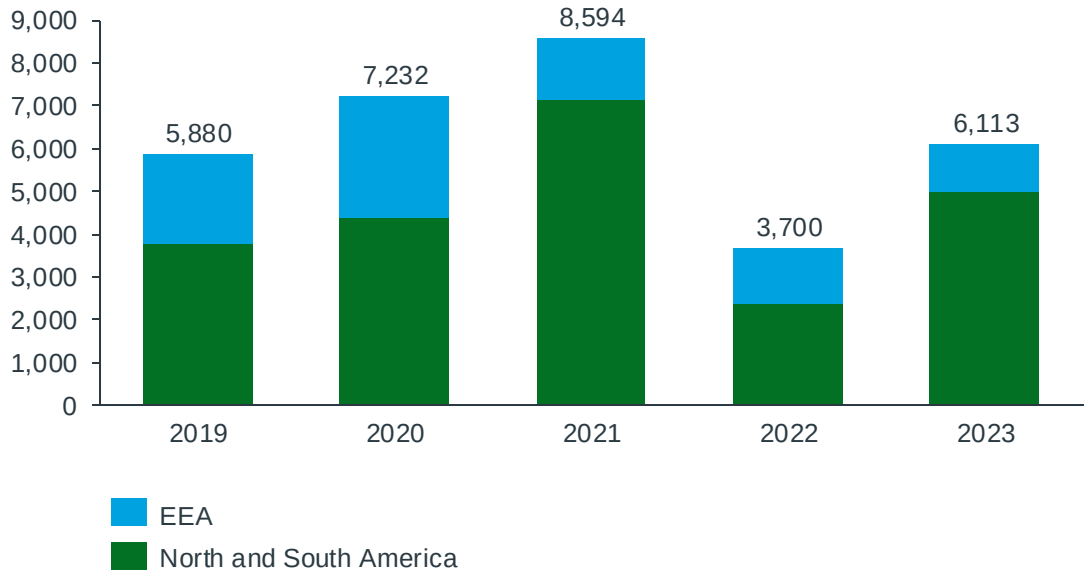
Share of rare diseases with and without approved treatment options



Approximately 30 million individuals in Europe are affected by rare diseases, and rare conditions are often associated with a high disease burden, with nearly 50% of cases diagnosed in early childhood

The development of new therapies is essential for improving patient outcomes, with clinical trials frequently serving as the primary option in the 95% of rare diseases with no approved treatments

Number of patients enrolled into rare disease trials EEA and North and South America in 2019-2023



Thousands of rare disease patients are receiving treatment options through clinical trials each year in the EEA and US, so a decline in rare disease trials would limit options for many patients

Note: Number of patients enrolled in rare diseases clinical trials: multi-country trials including sites in other than indicated regions were excluded
Sources: NORD Rare Disease; FDA, European Commission

Healthcare systems may miss out on revenue, cost-savings, clinical skills, and staff satisfaction associated with clinical trials

Impact on healthcare systems

Clinical trials bring direct financial benefit to healthcare systems through two mechanisms

- Revenue derived from running clinical trials
- Cost-savings associated with 'research-access' to innovative medicines

In 2018/19, the NHS received on average £9,000 per patient recruited to a commercial clinical trial and saved over £5,800 in drug costs for each of these patients. This equates to income of £355 million and cost savings of £28.6 million in 2018/19.

Scaled to EEA level, this suggests European health systems benefit from 1-1.5bn EUR from clinical trial payments and drug cost savings.

Based on studies of healthcare system performance, research and clinical trial activity is seen to impact:

Job satisfaction: staff involved in research have greater job satisfaction and staff turnover is lower in research active hospital groups

Clinical outcomes: research active hospitals have lower mortality rates (extending beyond research participants)

Healthcare performance: operational improvements have been seen from the creation of academic research placements

Clinical academic research is associated with **improved patient and carer experiences.**

Sources: Improvements in Medical Recruitment; Research Activity; HCP Collaborative Project ; Clinical Academic Activity

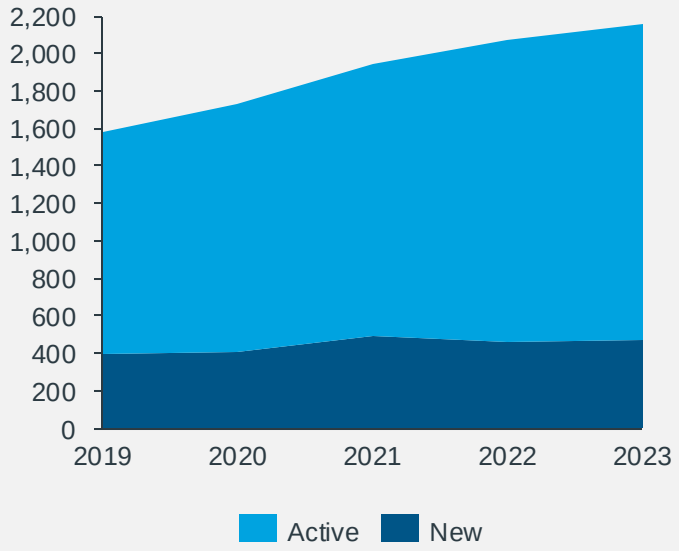
However, for sites able to capitalise on opportunities, clinical trials drive financial benefits and direct opportunities cutting-edge patient care

Impact on healthcare systems – Positive trends at a major Spanish site

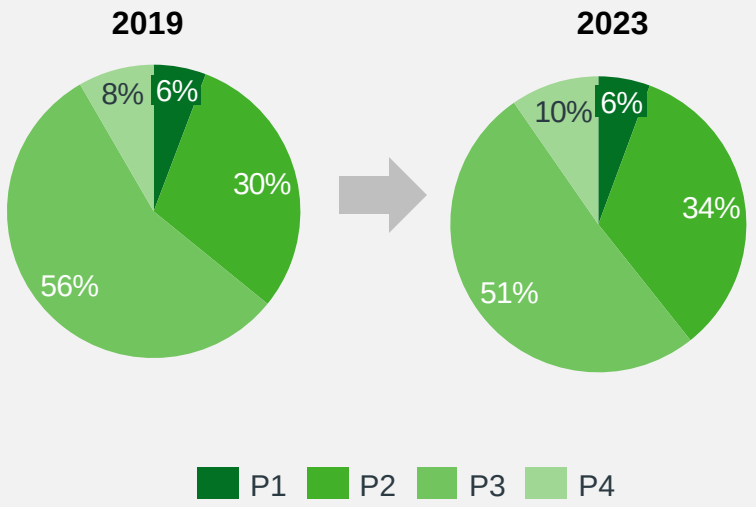
Vall d'Hebron is a major hospital and academic campus in Barcelona, seen as a leader in clinical research. **Contrasting to the wider EEA trend, the center has seen growth in clinical trials since 2019.** Hospital beds are located close to laboratories, supporting direct translation research. The center is viewed positively by industry leaders as a key site for trial delivery

Key statistics

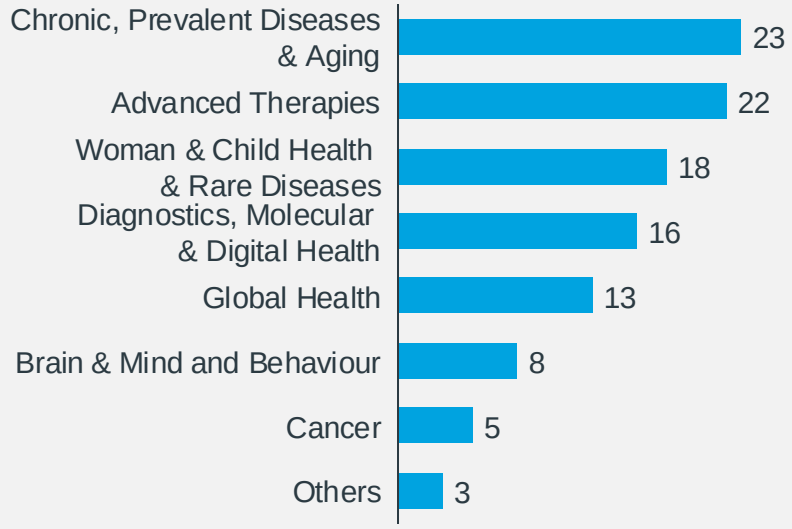
Active and new clinical studies per year



Trial split by phase



Trial split by TA group (%)



Sources: Vall d'Hebron

A thriving clinical trial ecosystem brings multi-billion Euro economic benefit, but requires coordinated government investment and policy implementation

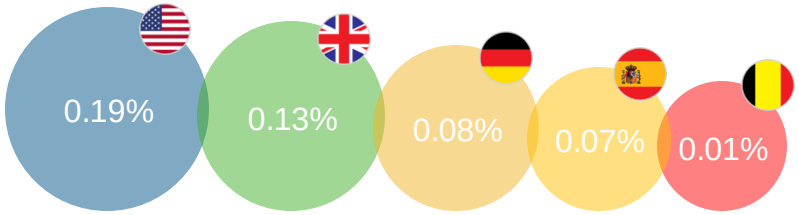
Impact on economy and society

Contribution to economic growth
in selected EEA and non-EEA markets

- **Based on a report in Denmark, EU clinical trials add +€130,000 to GPD per trial[1]**
- **A UK report estimates +£1.8 billion in gross value added (GVA)** to the UK economy, due to commercial clinical trials[2]

Clinical trial policy and investment cycle

Government health R&D Investment
in selected EEA and non-EEA markets



- **US government allocated 2x % GDP to health R&D than Germany and Spain,** and 19x Belgium, highlighting major variation in foundational support within and outside of Europe[5]

Private sector investment
in selected EEA and non-EEA markets

- In 2017, a **major CRO opened a 'Prime Site' in Barcelona (its first in Southern Europe)**, with a commitment to offer all trials run by the CRO to this Center. **This provides a major source of international trials to Spain[3]**
- **In UK, Singapore, Australia, a range of companies are developing vaccine manufacturing capacity, and committing to delivering local clinical trials through a range of public-private sector agreements[4]**

Clear policy and fast adoption
in selected EEA and non-EEA markets

- **Spain was the first in the EU country to adopt the Clinical Trial Regulation,** leading to a harmonization of national procedures and a greater commitment to rare disease and paediatric research[6]
- In 2023, to arrest declining clinical trial performance, UK committed to policy changes to reduce commercial clinical trial **approval times,** deliver a national approach to **trial contracting,** provide **'real-time' data on commercial clinical activity** in the UK, and establish a **common approach to contacting patients** about research

Sources: 1. Copenhagen Economics; 2. NIHR (UK); 3. Vall d'Hebron Hospital 4. (a) (b) (c) .5 Office of Life Sciences (UK); 6. Farmaindustria; 7. UK Government (Lord O'Shaughnessy review);

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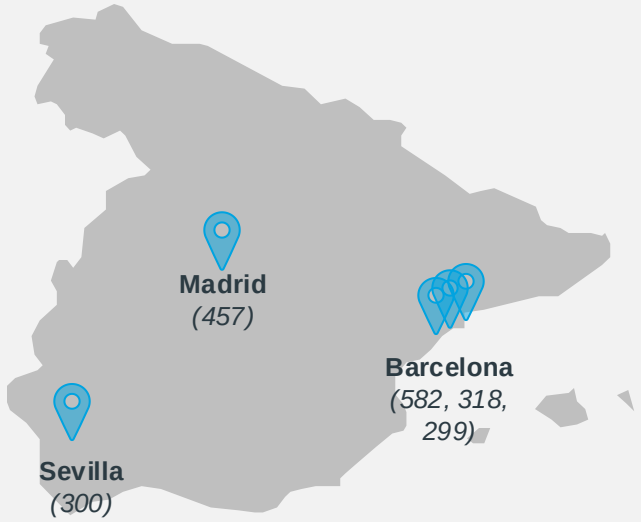
Spain is a strong EEA performer, with trials remaining stable and significant investment in key sites

Top 5 research centers in Spain
(number of ongoing trials)

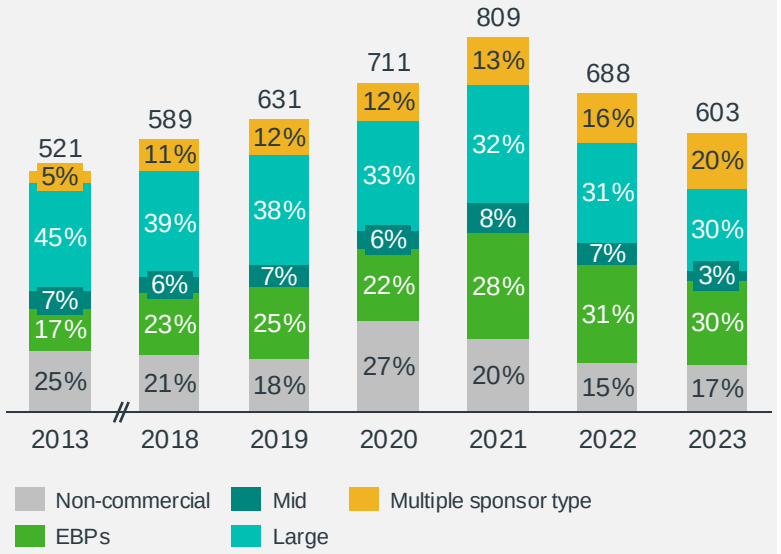


Spanish clinical trial sites in numbers

Total number of sites	Number of cities with sties
168	69

#trials per site	Initiated 2018-2024	Ongoing	Planned
Mean	105	61	2.25
Median	48	29	1

Clinical trial starts in Spain, by sponsor type



- **Over 80% trials** in Spain are sponsored by **commercial stakeholders** (higher than ~75% in EEA), with multi-sponsor **collaborations increasing**
- **Commercial clinical trials** represent an **investment of EUR 834 million in 2022** (60% of total R&D investment is the sector)*[1]

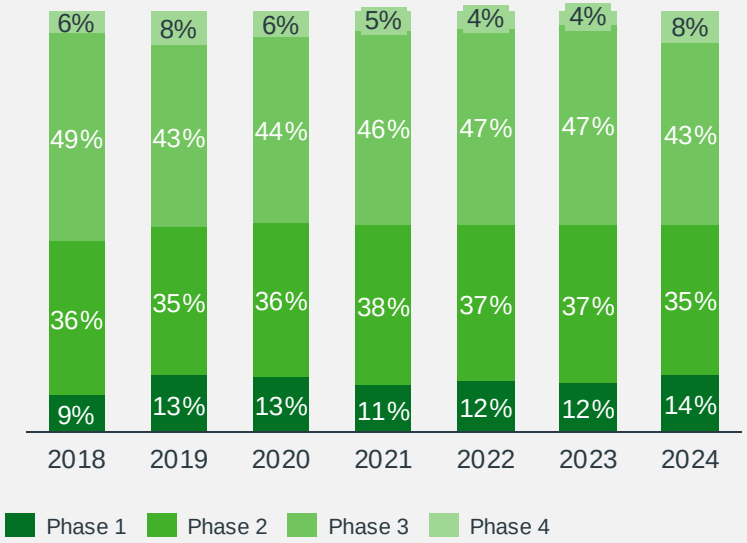
Country-specific insights

- Spain has taken a **proactive, coordinated, cross-stakeholder approach** to building its clinical trial ecosystem. Over the past decade, **investment in clinical trials has risen at an average annual rate of 5.7%**, climbing from EUR 479 million in 2012 to nearly EUR 834 million in 2022
- Factors attracting investment into Spain may include:
  - **Quality of Spain's healthcare system, e.g.,** hospital infrastructure
  - **Successful implementation of new European legislation** around clinical trials and adaptation of its own legislation accordingly
  - Effective **commercial/ non-commercial clinical trial collaboration model**
- **There are key research centers** in several major cities, and overall >**3 research centers per 10 000 km² area** of the country
- Within **immunisation,** excluding COVID-19 pandemic years, **~20 trials per year** are initiated in Spain

Note: FPI: first patient in; Top 5 research centres: holding the highest number of clinicals; *1 2018-2023 CAGR, commercial trials.
Sources: 1. PharmaBoardroom; 2. Clinical Trial Repository (Access Date: April 30th 2024)

Spain has shown broad therapy area growth, and faster than EEA average site-start up and recruitment timelines

Clinical trial starts in Spain, by phase



- Across last 6 years, the **phase distribution in Spanish clinical trials has been stable and follows EEA trends**
- A **slight increase in share** has been observed in **Ph1 and Ph4** trials

Top 10 TAs in Spanish clinical trials

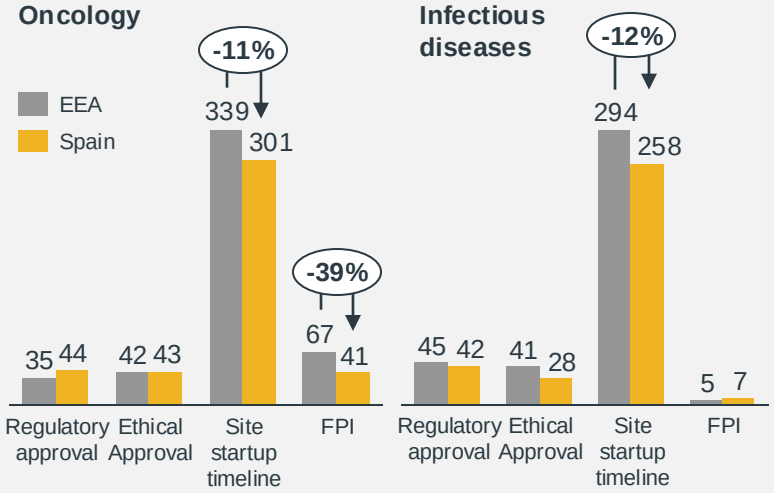
Therapy area	2018	2023	CAGR*
Oncology	216	186	-2%
Rheumatology	18	43	16%
Neurology	51	41	-4%
Cardiovascular	21	40	11%
Dermatology	29	33	2%
Respiratory	20	24	3%
Infectious Disease	23	23	0%
Medical Genetics – Rare	14	23	9%
Hematology	19	21	2%
Nephrology	11	19	10%

Positive CAGR | Stable CAGR | Negative CAGR

- Following global and EEA trends, **oncology remains the largest TA** in trials in Spain both in share and absolute numbers
- In line with EEA trends, both **oncology and neurology declined** over the last 6 years (2018-2023 CAGR: -2% and -4%, respectively)
- A **significant increase** has been observed in **CVD**, **nephrology** and **medical genetics – rare** (positive 2018-2023 CAGR 9-11%)

Clinical trial set up timelines in Spain and EEA

(Oncology: Spain: n>20, EEA: n>50)
(Infectious diseases: Spain: n>20, EEA: n>30)



- **Trial approval timeline** in both oncology and infectious diseases has been **comparable to EEA**, however **slightly lower within infectious diseases** (this might be attributed to accelerated approvals for COVID-19 trials)
- **Site startup timeline is faster in Spain** compared to average EEA timelines in both oncology and infectious diseases by 11-12%
- Time to **first patient in** within **oncology** trials is **significantly lower** (by ~40%) than mean EEA time

Note: FPI: first patient in; 2018-2023 CAGR, commercial trials.
Sources: 1. PharmaBoardroom; 2. Clinical Trial Repository (Access Date: April 30th 2024)

Denmark is a leading country in number of trials per capita, leveraging a relatively high number of research centres

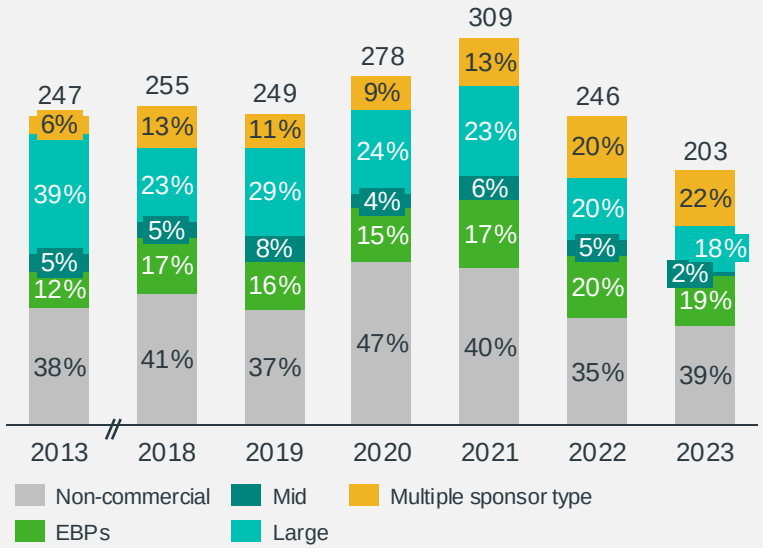
Top 5 research centers in Denmark
(number of ongoing trials)

Danish clinical trial sites in numbers

Total number of sites	Number of cities with sties
27	15

#trials per site	Initiated 2018-2024	Ongoing	Planned
Mean	37	24	2.25
Median	12	6	1.5

Clinical trial starts in Denmark, by sponsor type



- Overall, the **number of clinical trials in Denmark decreased** from 2018, though in line with EEA average
- In Denmark, **non-commercial** sponsors hold **significantly higher trial share** than average EEA share (~25%)
- **Trials held in collaboration** of multiple sponsors **increase** in share **reaching 22% in 2023**

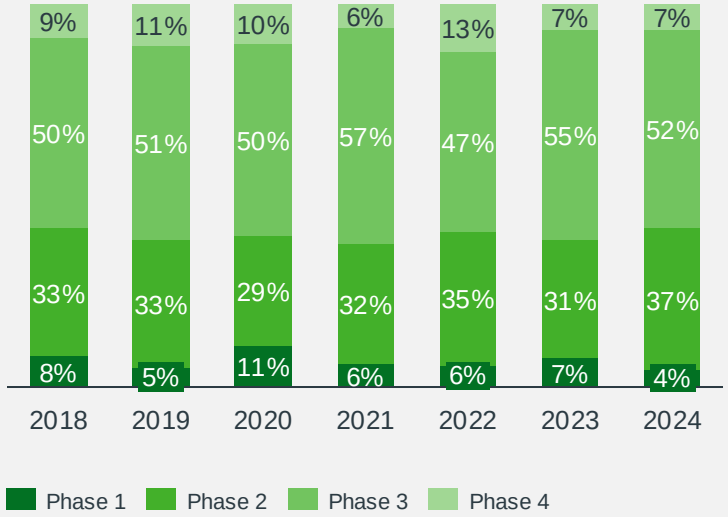
Country-specific insights

- Like Spain, **Denmark has taken proactive, cross-stakeholder actions to ensure the country is an attractive location for clinical trials**
- Denmark is perceived to have a strong clinical trial ecosystem, with relatively fast approval times, a range of clinical trial networks, and access to a range of real-world datasets to support patient-finding. Despite a fall in absolute number of trial starts in 2023, Denmark remains the **leading European country** in **number of clinical trial starts per capita**
- **Key research centers** in Denmark are evenly **distributed across the country** and overall there are **over 6 research centers per 10 000 km² area** of the country
- Within **immunisation,** excluding COVID-19 pandemic years, **10 trials per year** are initiated, a relatively strong performance given the country size

Note: FPI: first patient in; 2018-2023 CAGR, commercial trials.
Sources: 1. InvestinDK ; 2. Clinical Trial Repository (Access Date: April 30th 2024)

Therapeutic area trends in Denmark reflect EEA trends, and significant efforts have been made to meet target approval timelines under CTR

Clinical trial starts in Denmark, by phase



- Across last 6 years, the **phase distribution in Danish clinical trials has remained broadly consistent**
- In 2023, there was a drop in Phase 1 starts, mirroring a wider EEA trend

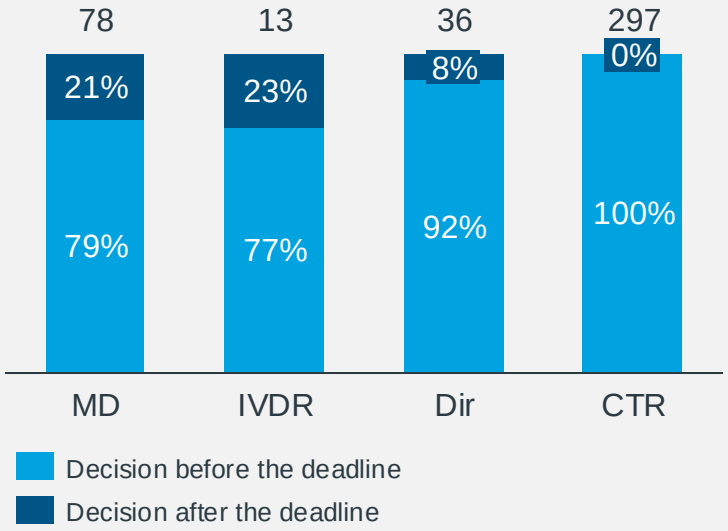
Top 10 TAs in Danish clinical trials

Therapy area	2018	2023	CAGR*
Oncology	47	37	-4%
Cardiovascular	11	18	9%
Neurology	18	13	-5%
Medical Genetics – Rare	7	11	8%
Endocrinology	10	10	0%
Rheumatology	2	9	28%
Dermatology	12	8	-7%
Respiratory	11	8	-5%
Nephrology	3	4	5%
Infectious diseases - vaccine	2	3	7%

Positive CAGR | Stable CAGR | Negative CAGR

- Following global and EEA trends, **oncology remains the largest TA** in trials in Denmark both in share and absolute numbers
- In line with EEA trends, both **oncology and neurology declined** over the last 6 years (2018-2023 CAGR: -4% and -5%, respectively)
- A **significant increase** has been observed in **rheumatology**, **CVD**, and **medical genetics – rare** (positive 2018-2023 CAGR 9-28%)

Clinical trial approval timelines in Denmark



- Denmark has taken steps to ensure clinical trial approvals are timely.
- In Denmark, **100% of clinical trial submissions** have been granted the decision within the estimated CTR timeline
- While the proportion of submissions processed within CTR timelines increased, the share of submissions processed within IVDR timeline slightly declined

Note: FPI: first patient in; 2018-2023 CAGR, commercial trials. Abbreviations: MD: Medical Devices, IVDR: In Vitro Diagnostic Medical Devices Regulation, Dir: previous clinical trial regulations, CTR: Clinical Trials Regulation
Sources: 1. PharmaBoardroom; 2. Clinical Trial Repository (Access Date: April 30th 2024) 3. De Videnskabsetiske Medicinske

Appendix

+ Further details on methodology

+ References

Data from the following Clinical Trial Repositories have been utilised in this analysis

Database	Region / Country
CT.gov	Global
EudraCT	EU
UMIN, JAPIC, JMAC	Japan
ISRCTN	Global
ANZCTR	Australia, New Zealand
IRCT	Iran
NTR	Netherlands
HKCT	Hong Kong
DRKS	Germany
ChiCTR	China
CTRI	India

Database	Region / Country
CRiS	Korea
NMRR	Malaysia
HAS CTR	Singapore
ReBec	Brazil
PHRR	Philippines
TCTR	Thailand
SRM CTR	Russia
Mexico CTR	Mexico
SLCTR	Sri Lanka
PACTR	Africa
RPCEC	Cuba

A range of other public sources have been referenced throughout this report

- IQVIA Institute Reports:
  - Strengthening Pathways for Cell and Gene Therapies
  - Rethinking Clinical Trial Country Prioritization
- Australia's Clinical Trials Sector
- European Commission: Europe's Beating Cancer Plan
- The impact of EU-CTR_An emergency signal from 2 large academic vaccine trial centers in Belgium_22MAY2024.docx (politico.eu)
- Distefar: Spain registers more than 900 clinical trials in 2022, above pre-pandemic levels
- TaylorWessing: Current developments in the field of clinical drug trials in Germany - adjusting parameters to shorten procedures before the start of a clinical trial
- Office of Life Sciences, UK Government
- The Association of the British Pharmaceutical Industry
- Clinical trial phase timelines
- NIH
- NORD: National Organisation for Rare Diseases
- FDA
- Rare diseases - European Commission (europa.eu)
- Improvements in Medical Recruitment
- Research Activity
- HCP Collaborative Project
- Clinical Academic Activity
- Vall d'Hebron
- Office of Life Sciences UK Government;
- UK Government;
- Copenhagen economics
- PharmaBoardroom
- De Videnskabsetiske Medicinske

In addition to the core metrics, a selection of other metrics were explored, but analysis was not included in this report given data limitations

Number and proportion of clinical trials terminated early and rationale

- Our initial data analysis suggests a decline in early terminated trials over last three years. Secondary sources[1] support this trend, showing:
  - A decrease in the number of trial terminations citing low enrolment. This may be due to improved patient engagement approaches
  - Despite this, low enrolment remains greatest source of termination, particularly in oncology and CNS, potentially due to increasingly narrow recruitment criteria
  - A growing proportion of terminated commercially sponsored trials now include a rationale, suggesting sponsors are becoming more transparent with this information

Number of first in human trials (FIH)

- First in human (FIH) trials are not widely coded in clinical trial registries
- Key word search (first in human', 'first in man') suggested a significant growth in FIH trials recent years, however this is inconsistent with secondary data sources, and therefore this metric has not been explored further in this report

Number of first in class trials (FIC)

- First in class (FIC) trials are not widely coded in clinical trial registries
- The FDA publishes an annual list of 'FIC' trials, whilst the EMA does not appear to publish equivalent information.
- Through this project, selected data has been collected from secondary sources, however this is metric has not been explored further in this report

Number of human challenge trials

- 'Human challenge' trials are not widely coded in clinical trial registries
- Number of human challenge trials (CHIM) were identified using key word search ('human challenge', 'controlled human infection model', 'CHIM') in titles of trials within ct.gov.
- The values do not align with other published sources e.g. PubMed studies, suggesting other data extraction methods are required
- This metric has therefore not been explored further in this report

Source: 1.