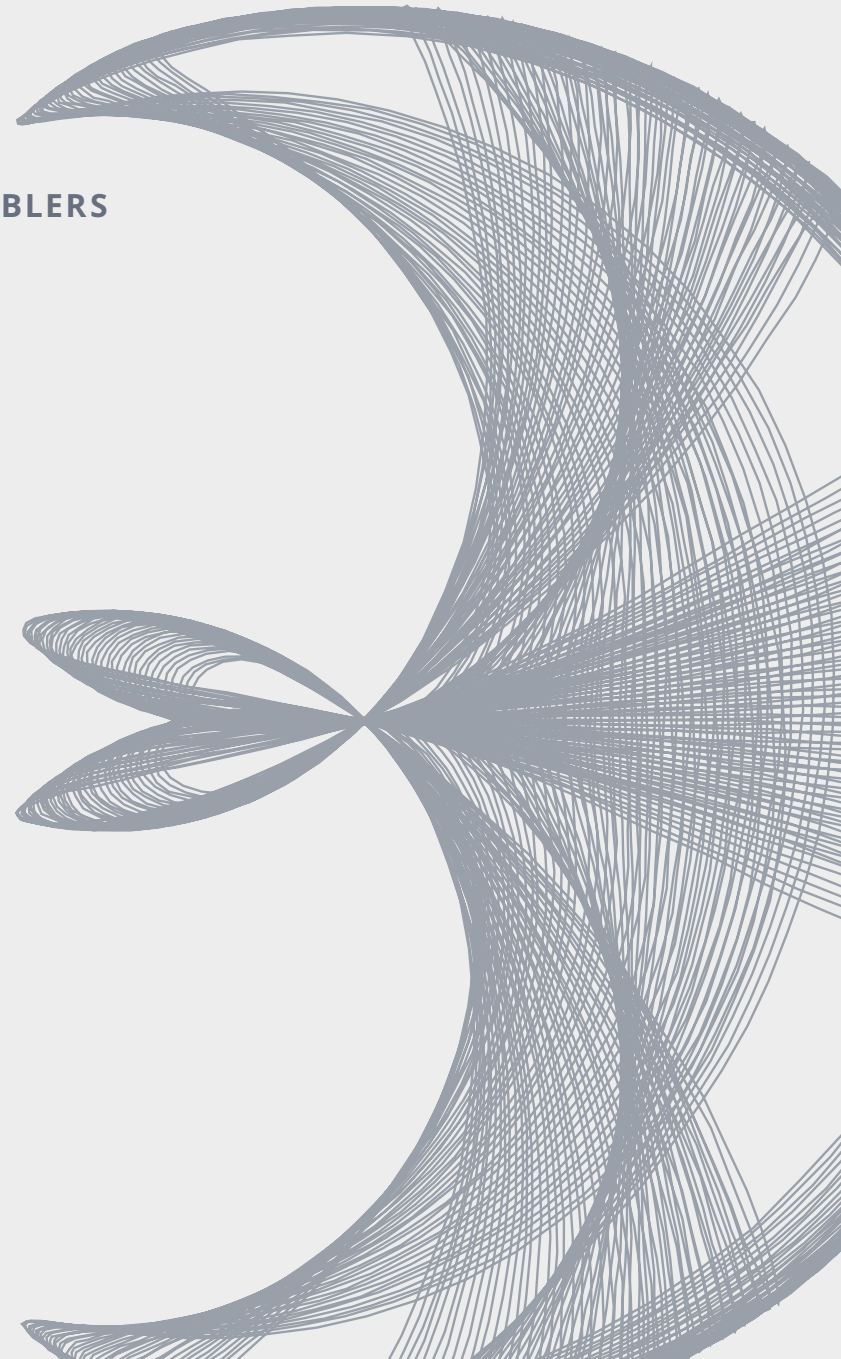
IQVIA INSTITUTE FOR HUMAN DATA SCIENCE

Global Trends in R&D 2023

ACTIVITY, PRODUCTIVITY, AND ENABLERS



FEBRUARY
2023

Introduction

As the global healthcare system re-equilibrates post-pandemic, the biopharmaceutical industry has resumed pre-COVID-19 levels of investment, pipeline activity, and launch of novel medicines following record breaking levels of each in 2020 and 2021. Process and technology innovations that were accelerated by extreme circumstances during the pandemic are being integrated across the global pipeline and implemented as operational and organizational changes that are enabling ongoing productivity gains.

This report assesses the trends in new drug approvals and launches, overall pipeline activity in terms of actively researched medicines, and the number of initiated clinical trials. It also profiles the state of R&D funding and the activity of companies of different types, and the results of research are compared to the input effort in a Clinical Development Productivity Index. This set of analyses reveals important shifts in therapeutic and geographic investments and ongoing prioritization of novel mechanisms of action, innovative development methods and accelerated regulatory pathways to optimize new therapy development and delivery to patients. This work also examines changes in the Productivity Index driven by shifting pipeline complexity and probability of success.

The research included in this report was undertaken independently by the IQVIA Institute for Human Data Science as a public service, without industry or government funding. The analytics in this report are based on proprietary IQVIA databases and/or third-party information and are not derived from proprietary sponsor trial information.

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MURRAY AITKEN
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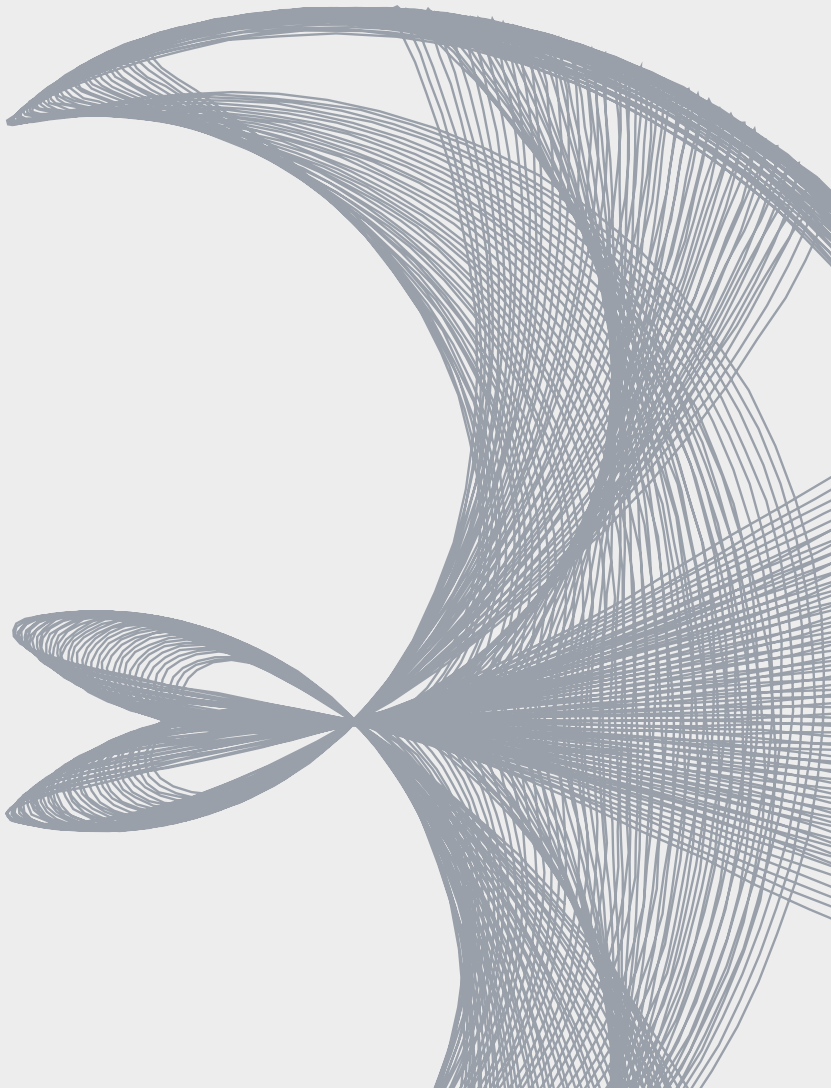


Overview

R&D FUNDING

The past year saw a restoration of pre-pandemic investment flows to life sciences companies in the U.S. after two years of heightened levels during the pandemic. U.S. focused biopharma investments declined 39% from a 2021 high, but at $42.1 billion, 2022 investments remain 25% above the $27.3 billion in 2019. Over the past five years, deal activity has shifted geographically to include more companies headquartered in China and Korea, and fewer Europe-based companies. While North American companies continue to execute the largest number of deals, these declined slightly over the five-year period.

R&D funding from the large pharmaceutical sector remained high with a record $138 billion invested in R&D by the 15 largest pharmaceutical companies in 2022. This represents an increase of 43% since 2017. The number of deals between pharma companies dropped by 25% from 2021 to 2022 with an increase in the share of deals involving emerging biopharma with larger companies.

R&D PIPELINE

The research and development pipeline remained flat in 2022 with 6,147 products in active development from Phase I to regulatory submission, with growth slowing to 2% over the last two years but maintaining an 8.3% CAGR from 2017–2022.

Oncology remains the focus of the pipeline, comprising 38% or 2,331 products and growing at 10.5% CAGR over the last five years with a recent shift to large-population solid tumor development contributing to the growth. Neurology continues to represent 11% of the pipeline, with research focused on Alzheimer's and Parkinson's, and increasingly depression and other mental health conditions.

Rare disease focus continues with more than 1,800 molecules targeting one of the growing number of rare disorders for which there are often no or very limited therapeutics available. Half of these focus on oncology, and next-generation biotherapeutics account for at least a quarter of the rare-oncology products, with increased activity in CAR T and NK cell therapies, as well as gene editing and nucleic acid vaccines.

Sources of industry scientific innovation continue to evolve with more than 2,800 companies or organizations currently contributing to the R&D pipeline. China-headquartered companies now account for 15% of the pipeline, up from 4% a decade ago, while Europe's and Japan's shares have fallen to 23% and 6%, respectively. Emerging biopharma companies (EBPs) are responsible for two-thirds of the molecules in the R&D pipeline, up from 51% in 2017 and one-third in 2002. U.S. and China-headquartered companies account for the largest share of the EBP pipeline at 46% and 20% respectively.

CLINICAL TRIAL ACTIVITY

Clinical trial activity was remarkably resilient even as the pandemic stretched through 2022, with a 2% decline in non-COVID-19 trial starts over 2021 and an increase of 8% over 2019 activity. COVID-19 trials, which surged dramatically in 2020, have dropped to less than half the 2020 level as the severity of the pandemic has subsided. 2022 saw a continued acceleration of mRNA vaccine trial activity led by continued focus on COVID-19 but expanding to meaningful development in multiple other disease areas.

Oncology remains the therapeutic area with the most clinical trial activity in 2022, accounting for 40% of trial starts. Within oncology, rare disease starts have been variably up and down in the past four years, while non-rare oncology has been consistently growing — oncology non-rare represented 44% of the oncology trial starts in 2022, which is the highest relative level in the past 10 years.

Many of the other therapeutic areas showed a slight decrease in clinical trial starts in 2022 versus 2021, but in most cases, remained close to 2019 levels suggesting a re-equilibration to pre-pandemic growth patterns. Exceptions to this include ophthalmology, women's health, and infectious disease where trial starts matched or slightly exceeded 2021 levels. Notably, though neurology dropped slightly, depression trial starts are 68% higher than pre-pandemic with novel mechanisms, including psychedelics, being tested in at least 35% of 2022 trials.

Across completed clinical trials, Black/African American and Hispanic patient representation has declined over the past decade — with Black/African American inclusion dropping 42% in the past two years — and remains below U.S. demographic levels for many therapeutic areas including cardiovascular, endocrinology, neurology, and oncology even in trials with only U.S. sites.

NEW DRUG APPROVALS AND LAUNCHES

A total of 64 novel active substances (NAS) launched globally in 2022, a decline from the more than 80 launched in each of the prior two years but representing a return to pre-COVID-19 levels. Declines were driven by fewer COVID-19 vaccines and therapeutics, fewer U.S. accelerated approvals, and fewer NAS launched only in China.

A growing share of new launches in 2022 were first-in-class, reflecting the increasing availability of novel science for patients. 2022 also saw continued growth in number of specialty medicine launches. As new medicines have increasingly targeted areas of high unmet need, clinical trial designs have used single-arm and open label designs and have been used in the approval trials for 43% of launches over the past 5 years.

A total of 353 novel active substances have launched globally in the past 5 years, bringing the 20-year total to 903, with variations in timing of launch and access to these medicines across major geographies. Emerging biopharma companies originated 67% of all new drugs in 2022 and launched 69% of those, indicating more independence on the part of these companies in taking products from innovation to market.

CLINICAL DEVELOPMENT PRODUCTIVITY

Based on the IQVIA Institute Clinical Development Productivity Index — which provides a composite metric of success rates, clinical trial complexity and trial duration — clinical development productivity increased dramatically in 2022 driven by a decrease in complexity as the pipeline moved away from large COVID-19 focused trials.

Specifically, the complexity metric returned to its pre-pandemic trend following a significant increase largely driven by very high subject enrollment across COVID-19 trials in 2021. The declining number of sites for rare diseases and oncology trials in 2022 is another key driver of the decrease in overall pipeline complexity.

The composite success rate across all therapy areas fell to 6.3% in 2022 while phase II and III success rates rose 2–6%. At the same time, trial durations have increased slightly over the past decade, though oncology and rare diseases trial durations have been declining in recent years, attenuating overarching trial duration increases.

PRODUCTIVITY ENABLERS

As technology and data innovations take hold across the pharmaceutical development pipeline, productivity is being impacted by a range of trade-off effects on complexity, timing and probability of success.

Scientific complexity continues to increase with first-in-class mechanisms in 62% of the launches spread across nearly all major therapeutic areas in 2022. Likewise, ongoing regulatory shifts are resulting in a rapidly evolving landscape for innovators.

Enablers including novel trial designs and remote, virtual or decentralized trials are playing an increasing role in the recent pipeline. Both advances in trial execution are associated with more subjects, sites, countries, and endpoints suggesting more complex execution, but both are expected to yield decreases in clinical program duration over traditional trials.

Most new drugs in 2022 received expedited reviews with increases in priority and breakthrough designations which, on average, include relatively fewer patients and therefore lower trial complexity. Additionally, the median time from first patent filing to launch for U.S. NAS remained near the lowest levels for the decade in 2022 at 11.2 years, in line with productivity enablers helping to bring industry development timelines down.

Looking forward, less ‘mature’ enablers are showing increasing potential for impact on clinical development productivity as evidenced by the advance of innovative AI/ML enabled research candidates into the clinical development pipeline.

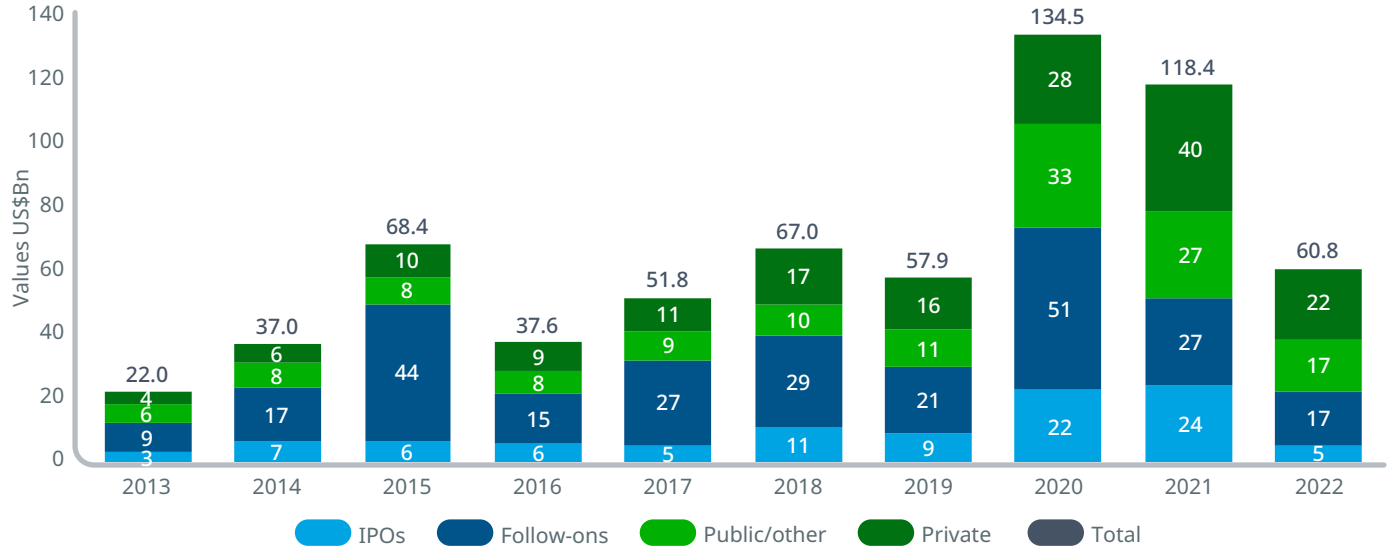
R&D funding

- Biopharma investment flows and deal activity in life sciences companies in the U.S. were restored to pre-pandemic levels after two years of heightened activity during the pandemic.
- Venture capital investments into U.S. companies declined 39% in 2022 but remain 25% above 2019 levels, while investments into European companies declined 74% in 2022 and are 47% below 2019 levels.
- U.S. venture capital deal activity and investment flows remain high at $42.1Bn, down from $54.8Bn in 2021 but above the $27.3Bn in 2019.
- Over the past five years, deal activity has shifted geographically to include more companies headquartered in China and South Korea and fewer Europe-based companies. While North American companies continue to represent the largest number of deals, they declined slightly over the five-year period.
- Deal activity in 2022 returned to pre-pandemic levels, with a 25% contraction of R&D collaboration versus 2019.
- The 15 largest pharmaceutical companies invested a record $138Bn in 2022 in R&D expenditure, an increase of 43% since 2017 and representing 18.8% of their recorded sales.
- The number of deals between pharma companies dropped by 25% from 2021 to 2022, with an increase in the percentage of deals involving emerging biopharma with larger companies.

The past year saw a restoration of pre-pandemic investment flows to life sciences companies in the U.S. after two years of heightened levels during the pandemic.

Biopharma funding levels slowed in 2022 but still exceed the 2019 level

Exhibit 1: Biopharma funding levels US$Bn, 2013–2022



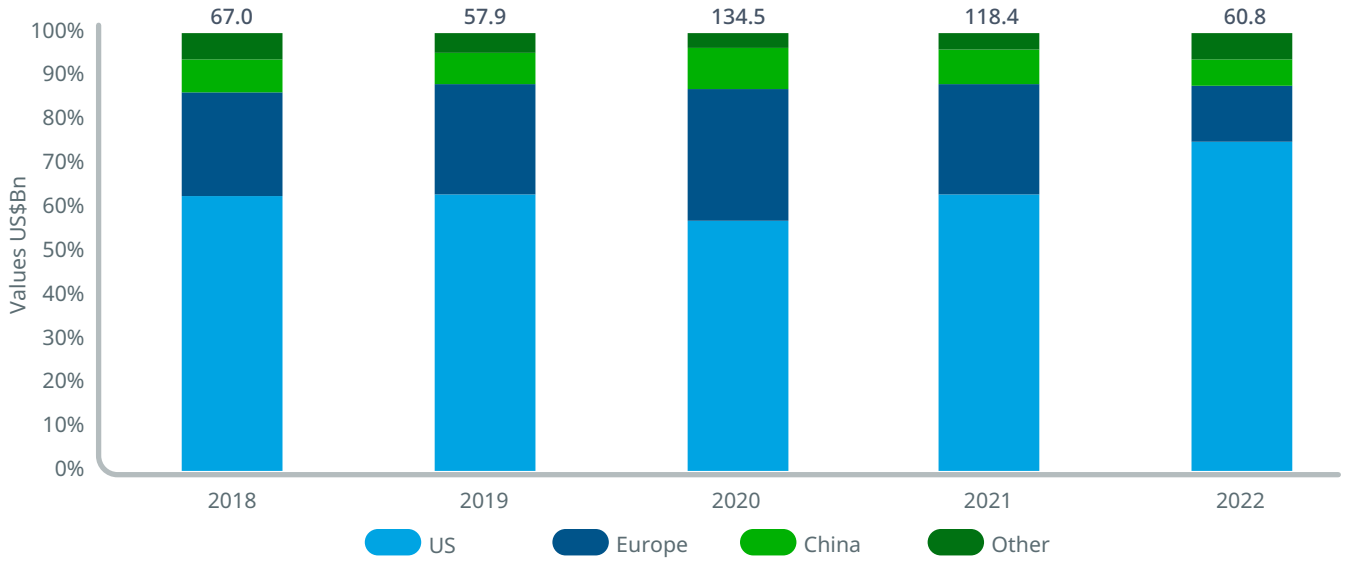
Source: BioWorld, accessed Jan 18, 2023.

- Biopharma funding including IPOs, follow-on funding, and venture capital investment slowed in 2022 after two years of heightened levels during the pandemic.
- The level of activity still exceeds the 2019 level, although the mix of funding types has shifted, and IPO activity was notably lower.
- The shifts in deal activity reflect changes in the types of companies being invested in, their therapeutic focus, and where they are located.
- Start-ups with a focus in COVID-19 had seen funding expand during 2020 and 2021 but slowed in the most recent months.
- Companies headquartered in China and Europe have seen deals slow more dramatically than those in the U.S.

Notes: Biopharma funding is related to a set of recipient companies globally defined by the Bioworld. IPO means initial public offering; Follow-on refers to a public offering of shares that is not the first one; Public/other financings are when public companies receiving financing in some other way; Private means venture capital investments.

Biopharma funding has shifted away from China and Europe in 2022

Exhibit 2: Biopharma funding levels by company location, 2018–2022



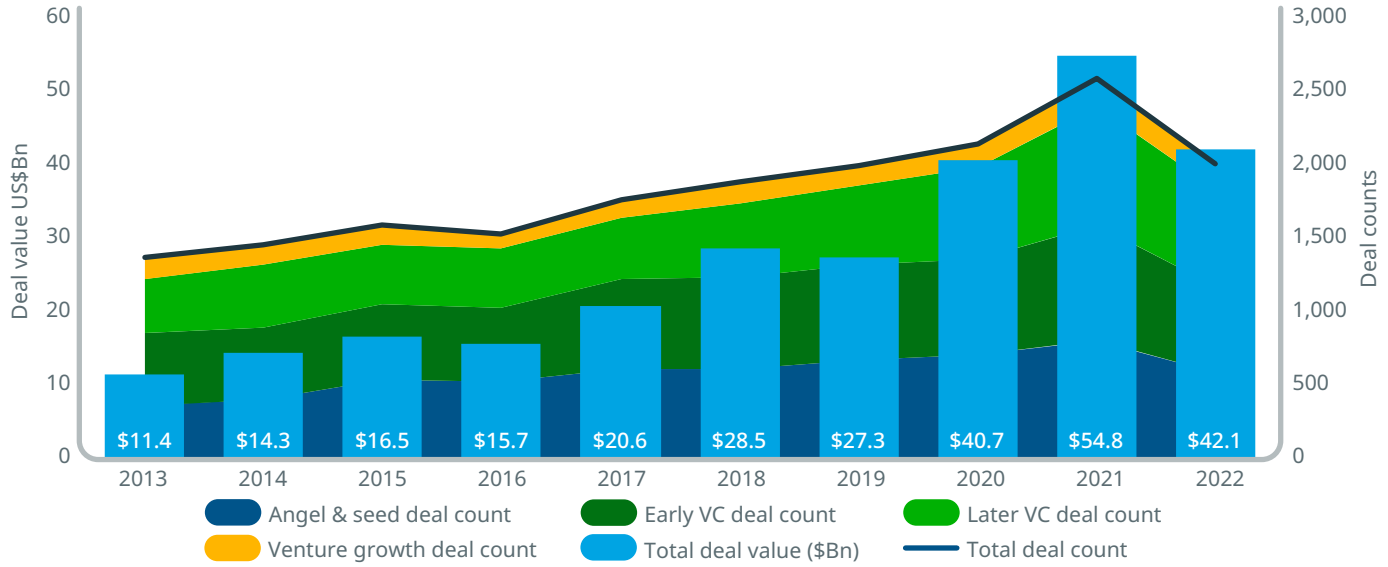
Source: BioWorld, accessed Jan 18, 2023.

- For companies receiving funding, those located in the U.S. rose sharply in 2020 and 2021, while dropping as a share of overall deals as a result of rising levels of funding in Europe, China and other countries.
- U.S. companies saw funding levels drop by 39% in 2022 compared to the prior year, while still being 25% higher than the 2019 level.
- European companies saw funding more than double in 2020 from the 2019 level but have seen that drop in the two years since. In 2018 and 2019, European companies received an average of $15.2Bn total funding, while the 2022 level is about half that level at $7.8Bn. The three-year average for 2020–2022 now exceeds $26Bn.
- Companies based in China saw their share of deals and absolute value jump in 2020 and 2021 and then drop by 59% in 2022 to a level that is 11% below the 2019 level.
- It remains to be seen if the 2022 share of deals by geography is a correction to unusual trends during the pandemic or a more sustained shift for these key hubs for innovation.

Notes: Biopharma funding is related to a set of recipient companies globally defined by the Bioworld. Company location is based on the recipient headquarters.

U.S. venture capital deal activity and investment flows remain high as interest in life sciences continues

Exhibit 3: U.S. life sciences venture capital deal value in US$Bn and number of deals closed by type, 2013–2022



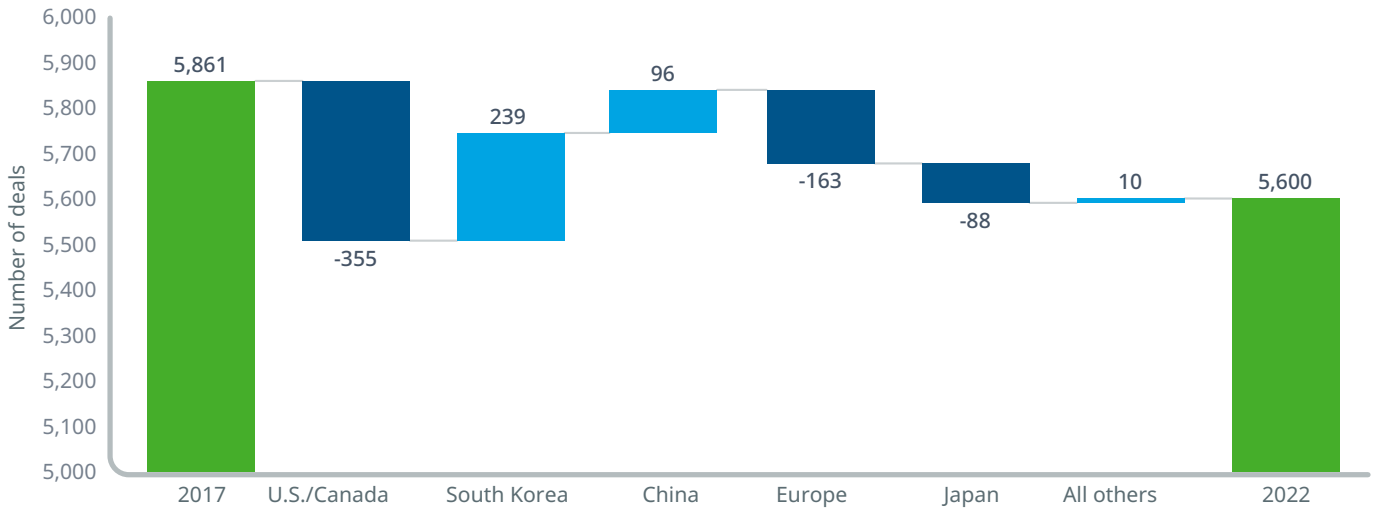
Source: PitchBook-NVCA Venture Monitor Q4 2022, accessed January 2023. Available from: https://pitchbook.com/news/reports/q4-2021-pitchbook-nvca-venture-monitor.

- Venture capital deal activity and investment flows in the U.S. accelerated in the past three years as interest in life sciences intensified, with more than 2,000 deals and $42Bn of deal value occurring in 2022, down from the level in 2021 but still far above pre-pandemic levels.
- Life sciences venture capital deals continue to grow, with an uptick in investment in later-stage deals which typically draw more dollars and show a 10% CAGR increase since 2017 compared to only 5% CAGR for the five years through 2019.
- The total number of deals peaked at 2,588 in 2021 — 21% higher than 2020 — but dropped 22% in 2022 to 2,009 deals, only slightly above the 1,994 in 2019.
- Deal value jumped in 2020 and has remained elevated since, with 2022 at $42.1Bn, 54% higher than the 2019 level.
- The escalation of deal value in 2020 and into 2021 represents a significant shift in trajectory and reverses a flat-to-declining trajectory from 2018 to 2019.
- The number of angel and seed deals dropped sharply in 2022 to 586 after higher deals of 710 and 799 in the prior two years, far above the previous trend.

Notes: U.S. Life Sciences venture capital funding deals is more inclusive than global biopharma analysis in earlier exhibits by including only U.S.-based companies as well as including life sciences companies in adjacent sectors including service providers to involved companies, drug distribution, care delivery, and insurers. VC = Venture Capital. Deals involve companies defined as life sciences which includes a range of biopharma, healthcare delivery and distribution and other types of company.

Deal activity has significantly increased in Korea and China over the past five years with US, Europe and Japan declining

Exhibit 4: Change in deals involving companies headquartered in various geographies, 2017–2022



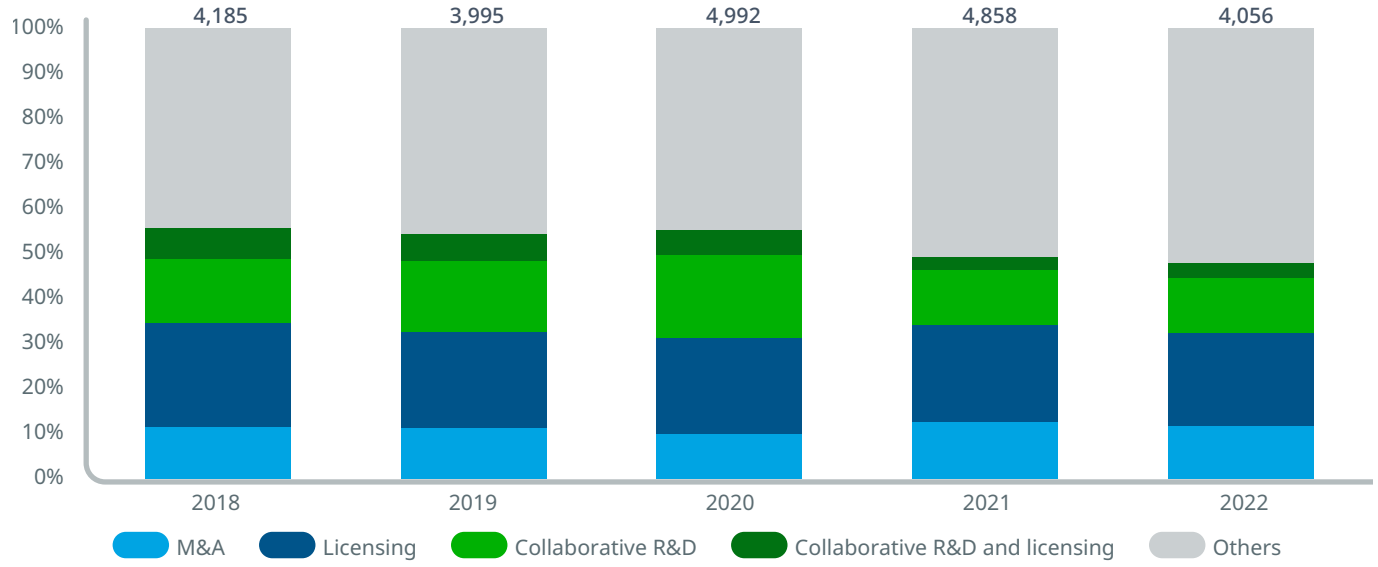
Source: IQVIA Pharmadeals, Dec 2022.

- North America represents the largest global cluster of life sciences entrepreneurship and as a result includes 57% of deals in 2022, dropping from 62% in 2017. Total deals between companies involving the region dropped by 355 or 13% over the five-year period.
- Since 2017, the level of deal activity has shifted considerably, with rising activity from companies headquartered in South Korea and China.
- There were 387 total deals in China in 2022, up 33% from five years earlier, reflecting a significant increase in the level of interest in the innovations from these companies and many including high profile large pharma collaborations or licensing deals, and the near-term expectation that some of these medicines will be approved in the U.S. and other major developed markets.
- The increasing deal volume with South Korean companies is greater than with Chinese companies, growing from 251 five years ago to 490 in 2022, but involving a greater share of licensing and collaborative R&D deals building on the established biologic and biomarker capabilities of key companies along with well placed regional capacity for manufacturing, including biosimilars.
- Deals involving European companies dropped by 163 or 9%, while share of activity dropped from 41% to 39% as the rate of activity failed to keep pace with the increases from the more active Asian companies.

Notes: Deals by company headquarter location between pharma companies and are not mutually exclusive. Total deals include double-counts of deals where participants are in different regions. Excludes venture capital and funding deals. Funding deals are defined as those which include grants and awards from governments, etc.

2022 deal activity returned to pre-pandemic levels with a 25% contraction of R&D collaboration versus 2019

Exhibit 5: Number of life sciences deals and share by type, 2018–2022



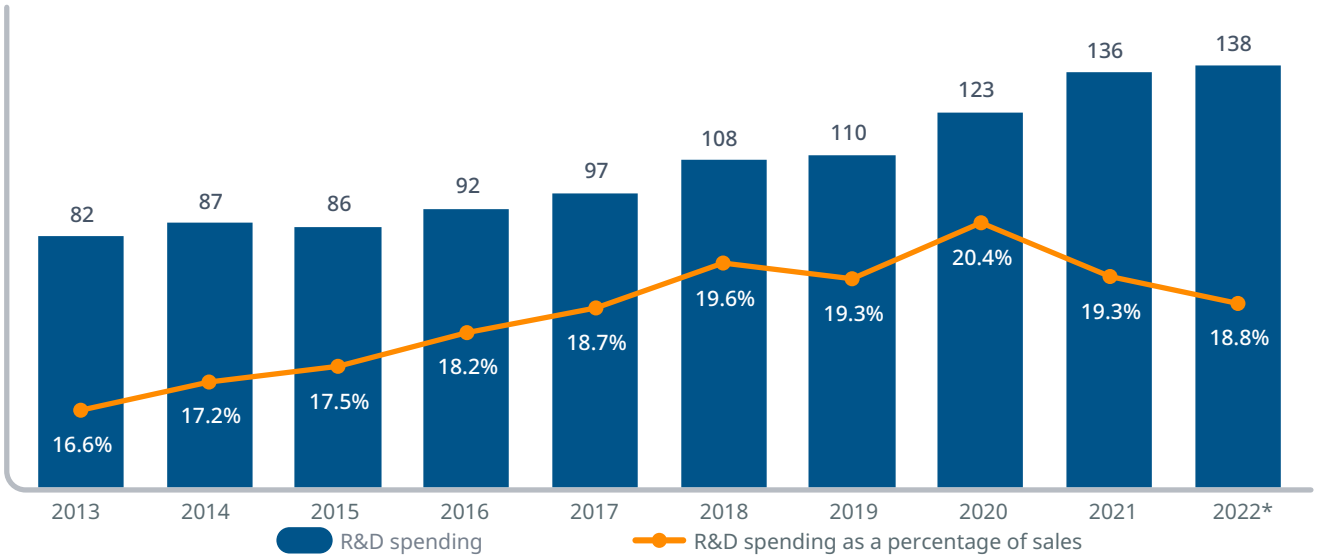
Source: IQVIA Pharmadeals, Dec 2022.

- Overall, there was a decrease in activity across all deal types in 2022, driven by hesitancy toward dealmaking related to geopolitical tensions, drug pricing and macro-economic issues (fluctuating valuations, inflation).
- Publicly disclosed life sciences deal activity reveals that the number of agreements signed in 2022, excluding standalone research grants, was approximately 1.5% above the 2019 level and 16.5% lower than 2021.
- In 2021 there were 519 COVID-19-related deals, dropping to 286 in 2022 as there were fewer perceived new opportunities in either vaccines or therapeutics.
- While the rising number of deals was driven by COVID-19 in 2020 through 2022, the 4,339 non-COVID-19 deals in 2021, were 9% higher than 2019, and the 3,770 non-COVID-19 deals in 2022 was 6% lower than 2019, reflecting a return to previous trends.
- General market volatility and prospect of increased regulatory scrutiny led to a significant cooling of appetite for M&A deals.
- The M&A process had initially been reported to be hindered by a lack of face-to face contact, particularly for larger deals, which resulted in delays but did not stop the signing of new deals. Much of the industry had returned to in-person meetings at many conferences in 2022.
- There were 483 M&A deals announced in 2022, down from 615 in 2021 (defined here as Mergers, Business Acquisitions and Divestments, signed but not necessarily completed) but matching the number in 2018.

Notes: Life sciences deals disclosed and categorized by type, excluding funding deals.

R&D expenditure by large pharma corporations totaled a record $138Bn in 2022*, an increase of 43% since 2017

Exhibit 6: Large pharma R&D spending and spending as a percentage of sales 2013–2022*, US$Bn



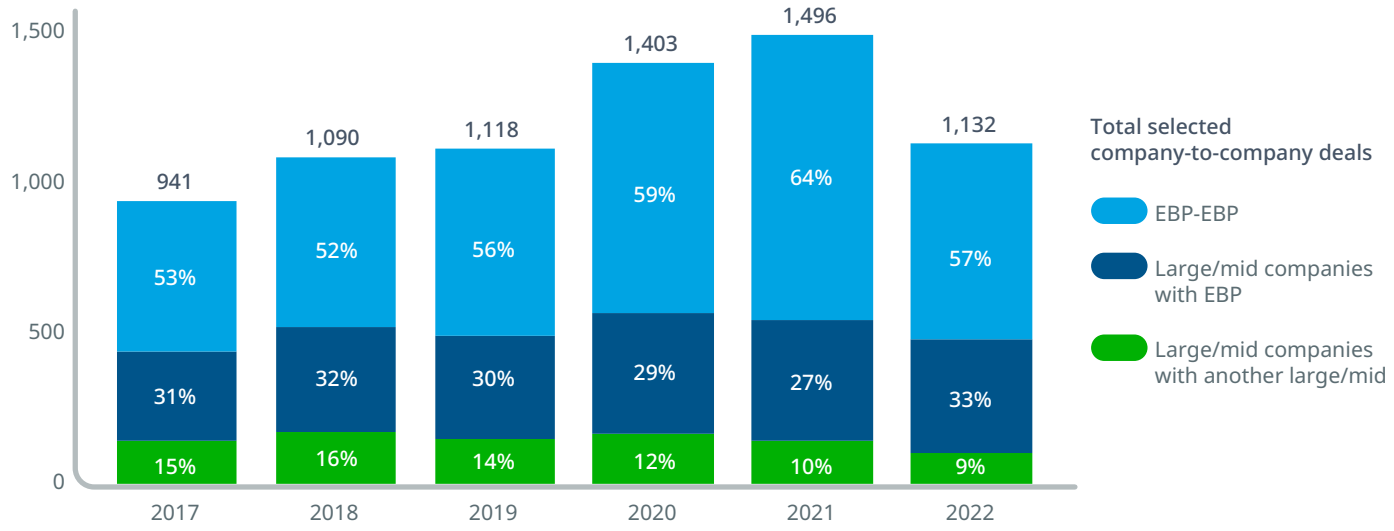
Source: Company financial statements; IQVIA Institute, Jan 2023.

- The largest pharmaceutical companies together spent more than $138Bn on research and development in 2022, up 1.7% from 2021.
- Across these companies, R&D dropped to 18.8% of revenue in 2022 after four years above 19% but remains at historically high levels.
- Global revenue for these 15 companies totaled $737Bn in 2022, up from $704Bn in 2021, a 4.7% increase in net sales.
- The reduction in R&D % of revenue in 2022 is attributed to fewer companies having major write-offs from failed R&D programs, and some large companies having a major increase in sales related to COVID-19 vaccines or therapeutics while their R&D spending also increased, but at a slower rate.
- Since 2017, R&D spending for large companies has increased by 43% with a five-year CAGR of 7.4%.
- R&D expenses can include write-offs of failed R&D programs developed internally or acquired, which can bring year-to-year variability in the level of total spending.

Notes: *Based on financial reporting for twelve months ending Sep 30, 2022 for all companies except Roche which is based on 12 months ending Jun 30, 2022. All other years reflect total R&D for the calendar year indicated. CAGR = Compound annual growth rate. Companies include: AbbVie, Amgen, AstraZeneca, Bristol Myers Squibb, Eli Lilly, Gilead, GlaxoSmithKline, Johnson & Johnson, Merck, Novartis, Novo Nordisk, Pfizer, Roche, Sanofi, and Takeda. These represent the total company view, and some divisions such as consumer health are typically less R&D-intensive than the pharmaceutical division. The total expenditure is as reported by companies in their financial statements.

Deals between pharma companies dropped by 25% from 2021 to 2022, mostly in EBP-only deal activity

Exhibit 7: Number and share of deals by company segment, 2017–2022



Source: IQVIA Pharmadeals, Dec 2022.

- Emerging biopharma companies - defined as those with less than $200Mn in R&D spending and less than $500Mn per year in annual sales — have expanded their involvement in deals steadily over the past five years.
- In 2017, large and-mid-sized companies — those with more than $5Bn in global sales — were involved in 46% of deals that involved other large and mid-sized or emerging companies; while that level of deals has remained steady, as a share of the company deal activity, it has dropped to 42%.
- The shifts in activity over the past five years have meant that 90% of all deal activity between these types of companies involves an emerging company, up from 84% five years ago, even as the activity between emerging companies without a larger firm now represent 57% of deals, up from 53% five years ago.
- The rising independence of emerging biopharma companies in recent years, shifted in 2022 as deals involving larger companies jumped from 27% in 2021 to 33% in 2022.
- Even so, novel drugs developed by emerging biopharma are also being launched by them more often, with 69% of the 26 EBP-originated NAS launches in the U.S. in 2022 also being launched by an EBP (Exhibit 31).

Notes: Deals in this analysis exclude funding deals. Funding deals are deals that involve research grants or funding from government institutions, government bodies, universities or other academic institutions. Excludes VC and funding grants from non-commercial.

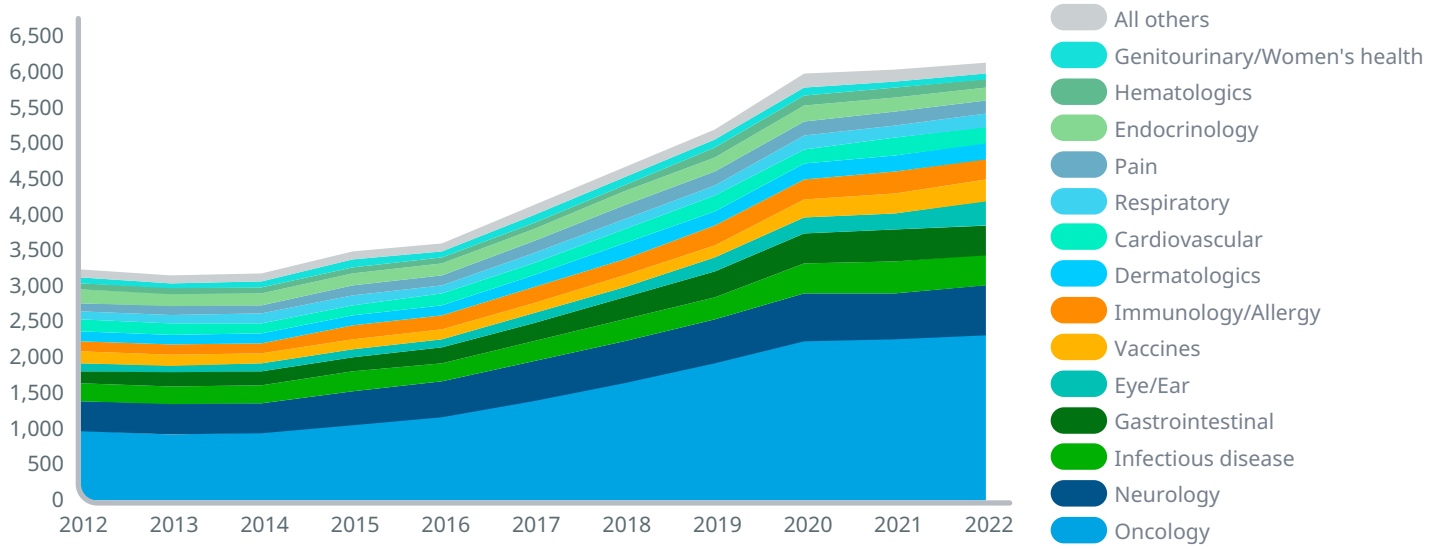
R&D pipeline

- The research and development pipeline remained flat in 2022, with 6,147 products in active development from Phase I to regulatory submission, growing 2% over the last two years, but 49% since 2017.
- The clinical development pipeline for non-rare cancers grew 7% in 2022, however development for rare cancers has plateaued or declined slightly since 2020, which may reflect the beginning of a shift away from rare cancers by pharmaceutical companies.
- Oncology development is focused more on solid tumors, with 5% growth over the last year, while development of drugs for hematological cancers declined 4% in 2022.
- Neurology research is focused on Alzheimer's and Parkinson's, with depression and other mental health conditions becoming increasingly more important.
- The focus on rare diseases — beyond rare cancers — is reflected in the R&D pipeline, which includes more than 900 molecules targeting one of the growing number of rare disorders for which there are often no or very limited therapeutics available.
- More than 900 next-generation biotherapeutics are now in the R&D pipeline, with increased activity in CAR T and NK cell therapies as well as gene editing and nucleic acid vaccines. More than 40% of next-generation biotherapeutics in development in 2022 were for oncology, bringing great promise for cancer treatment.
- More than 2,800 companies or organizations currently contribute to the R&D pipeline. China-headquartered companies now account for 15% of the pipeline, up from 4% a decade ago, while Europe and Japan's shares have fallen to 23% and 6%, respectively.
- Emerging biopharma companies (EBPs) — defined as those with R&D spending less than $200Mn per year and less than $500Mn in annual sales — are responsible for two-thirds of the molecules in the R&D pipeline, up from 51% in 2017 and one-third in 2002.
- Emerging biopharma drug development is rising rapidly, particularly in China-headquartered companies, whose share now exceeds that of Europe. U.S.-headquartered companies represent nearly half of EBP development, while Europe and Japan have seen declining shares of the EBP pipeline over the last decade.

The research and development pipeline remained flat in 2022 with ongoing oncology focus and continued share gain in rare, next-generation, Chinese and EBP segments of the pipeline.

Growth in the clinical pipeline has remained flat since 2020, although 49% above 2017 levels

Exhibit 8: Number of pipeline products Phase I to regulatory submission by therapeutic drug class, 2012–2022



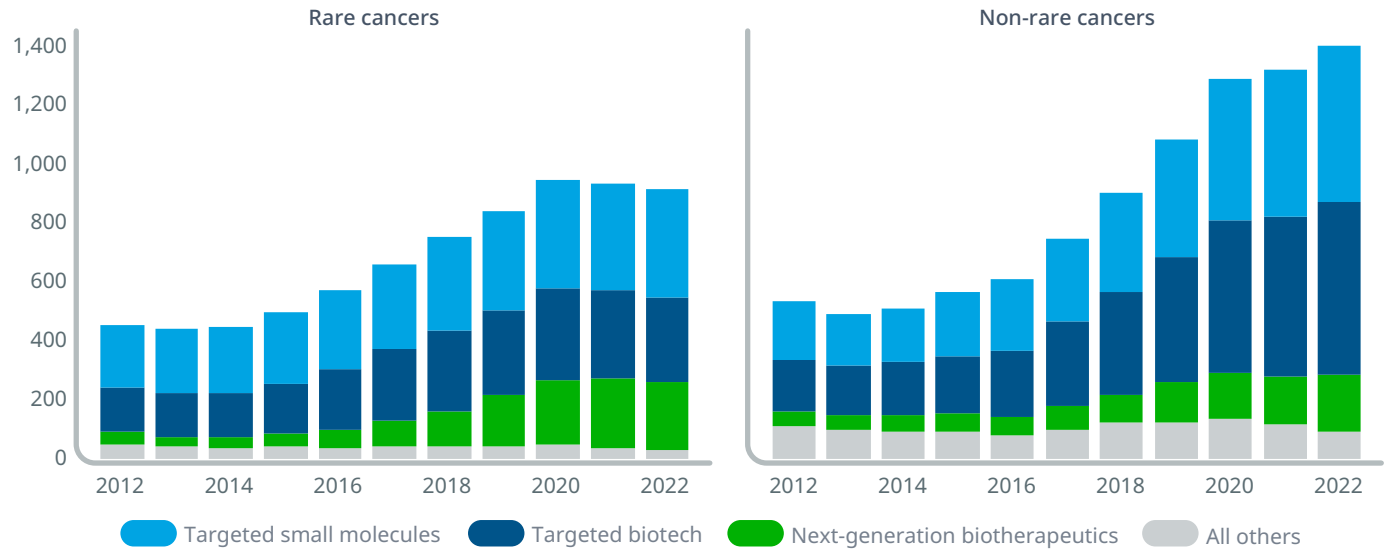
Source: IQVIA Pipeline Intelligence, Dec 2022; IQVIA Institute, Jan 2023.

- The research and development pipeline remained flat in 2022, with 6,147 products in active development from Phase I to regulatory submission, growing 2% over the last two years and 49% since 2017.
- This slowing growth since the pandemic began is likely due to delays in development activity as COVID-19 and new variants have caused a series of disruptions to society since 2020.
- Oncology remains the focus of the pipeline, comprising 38% or 2,331 products and growing at 10.5% CAGR over the last five years.
- Neurology continues to represent 11% of the pipeline, with growth in the number of products in development to 699 following a modest decline in 2021.
- The therapy area with the highest CAGR since 2017 is eye and ear conditions (20.7%), which is predominantly focused on ocular anti-neovascularization products and treatments for rare eye conditions.
- Vaccines have the second-highest CAGR since 2017 (14.1%), with a heavy focus on COVID-19 vaccines and influenza in recent years.
- Products in development for gastrointestinal disorders account for 7% of the pipeline, growing 9.9% CAGR over the last five years. There has been an increased focus on rare gastrointestinal conditions and liver disease.

Notes: Includes drugs with an active research program, with phase determined by the highest phase of research regardless of indication. Oncology includes supportive care. Neurology includes central nervous system disorder treatments and mental health treatments but does not include pain management or anesthesia.

The clinical pipeline for large population cancers continued to grow in 2022, while rare cancers peaked in 2020

Exhibit 9: Number of Phase I to regulatory submission oncology pipeline products by type, 2012–2022



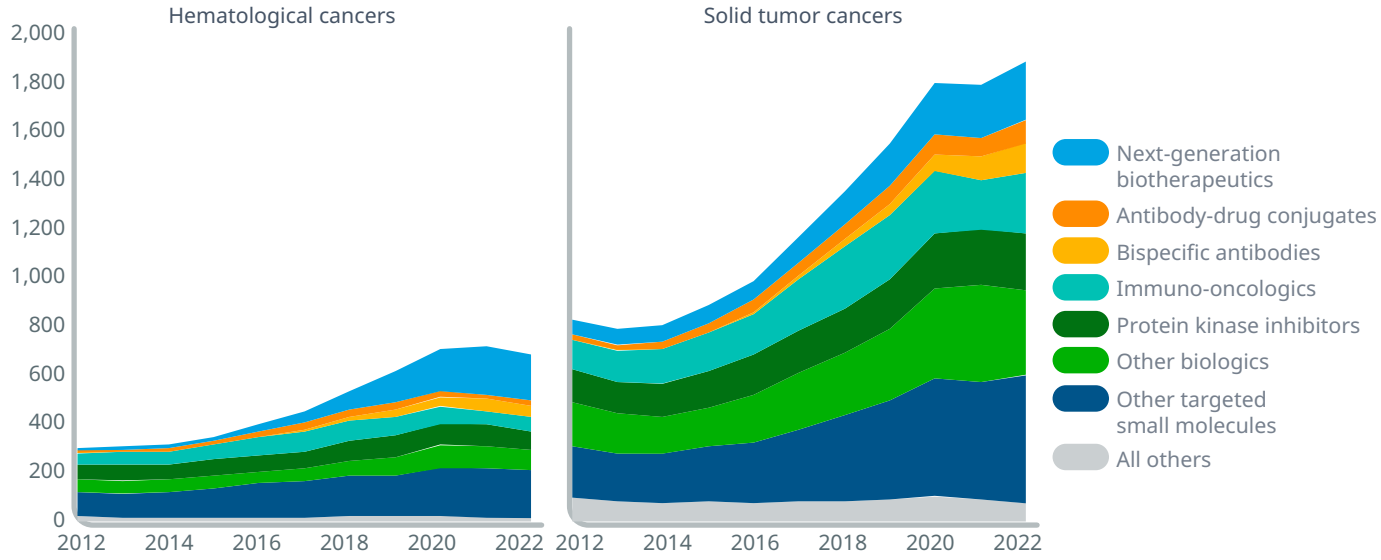
Source: IQVIA Pipeline Intelligence, Dec 2022; IQVIA Institute, Jan 2023.

- The clinical development pipeline for non-rare cancers grew 7% in 2022, however development for rare cancers has plateaued or declined slightly since 2020, which may reflect the beginning of a shift away from rare cancers by pharmaceutical companies.
- In 2022, 39% of the oncology pipeline was under development for rare cancers, down from 41% in 2021 and 46% five years ago.
- Targeted small molecule and biotech therapies continue to grow in development for non-rare cancers but have seen limited growth and even declines in rare cancers. These include many of the new immuno-oncology treatments, checkpoint inhibitors, and kinase inhibitors.
- Although next-generation biotherapeutics represent a smaller share of the total oncology pipeline, these cell, gene, and RNA therapies provide promising tools for more precision in cancer treatment, particularly in rare cancers where one-quarter of products under development are next-generation.
- As many of these targeted or next-generation treatments relate to genetic mutations or other biomarkers, the use of companion diagnostics is likely to become more prevalent to provide more precise and effective treatment in cancer patients.

Notes: Analysis includes medicines in active research with a focus on cancer therapeutics including supportive care. Medicines are considered targeted if their mechanism of action uses a specific biomarker to target treatment within the body. Many cancer drugs have multiple tumors in research, and drugs which have any trials focused on rare cancers have been included as rare. Drugs which have no rare tumor targets are considered non-rare. All other includes a range of cytotoxic, hormonal, and radiotherapeutic mechanisms without a targeting mechanism.

Oncology development is focused on solid tumors, with next-generation biotherapeutics growing across all cancers

Exhibit 10: Oncology R&D pipeline Phase I to regulatory submission by type, 2012–2022



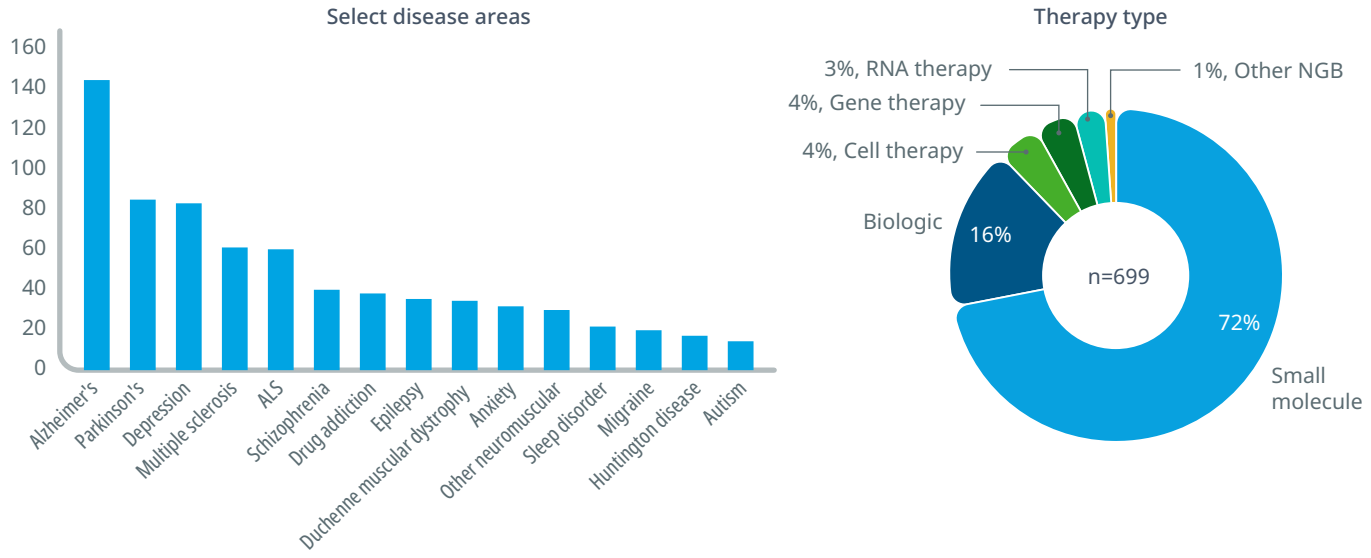
Source: IQVIA Pipeline Intelligence, Dec 2022; IQVIA Institute, Jan 2023.

- Oncology research and development has seen an increasing focus on targeted drugs, with innovative mechanisms of action for treatment of cancers over the last decade.
- While development of drugs for hematological cancers declined 4% in 2022, clinical development for solid tumor cancers grew 5% following a slight contraction in the pipeline in 2021.
- Next-generation biotherapeutics are increasingly under investigation for hematological cancers, with the number of products currently in active research more than four times what it was in 2017 and accounting for 28% of the hematological-oncology pipeline.
- Immuno-oncologics, which saw significant growth over the last decade, have begun to taper off in recent years, with declines in hematological cancers beginning in 2018 and in 2019 for solid tumors, potentially indicating a switch to even newer targeted molecules.
- Despite being first developed in the 1960s, bispecific antibody development for cancer treatment was minimal a decade ago and has grown significantly, now representing 7% of both the hematological-oncology and solid tumor pipelines, indicating an increasing focus on the ability of these molecules to act on multiple targets or through different mechanisms of action.
- Many new antibody-drug conjugates have been under development in oncology in the last decade, allowing for targeting cytotoxic agents directly to cancer cells, improving on the non-specificity of older oncology products.

Notes: Other includes non-targeted mechanisms within categories of cytotoxics, hormonal, and radiotherapeutics. Products being investigated for more than one type of cancer may be included in both hematological and solid tumor cancers.

Neurology research is focused on Alzheimer's, Parkinson's and depression, with a range of other often rare diseases

Exhibit 11: Number of products in neurology Phase I to regulatory submission pipeline in 2022 by disease and therapy type



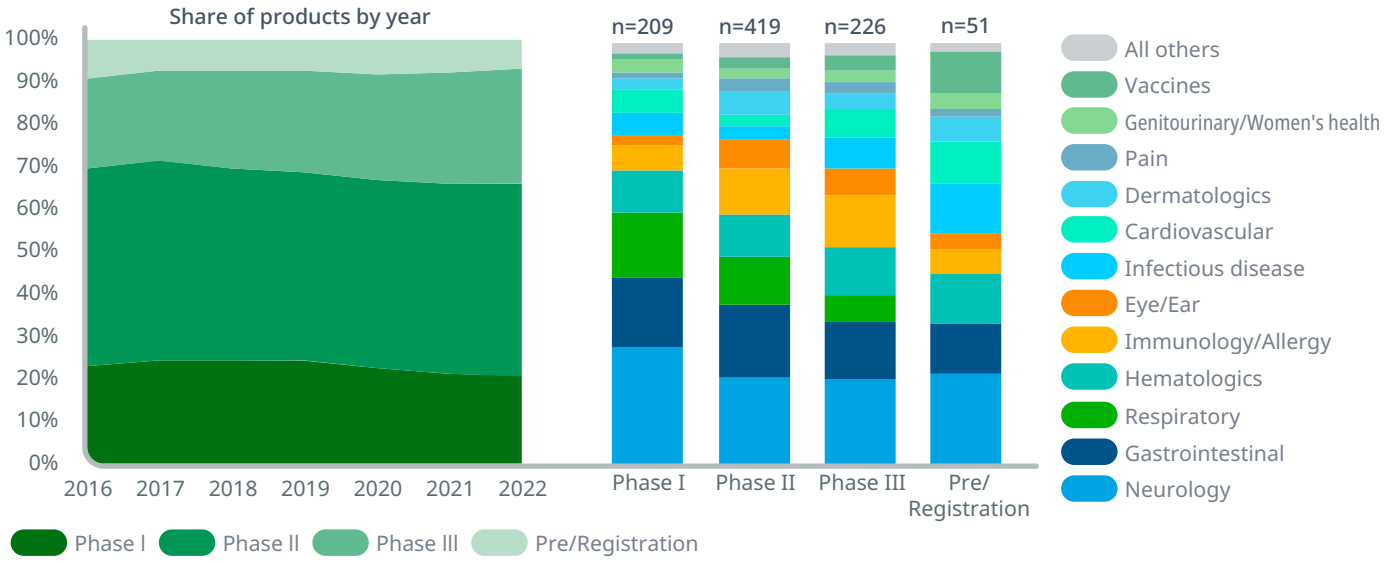
Source: IQVIA Pipeline Intelligence, Dec 2022; IQVIA Institute, Jan 2023.

- There are currently 699 products under investigation in the neurology pipeline, including products to treat neurodegenerative, neuromuscular, and psychiatric disorders.
- Much of the ongoing research is focused on Alzheimer's and Parkinson's diseases, with 127 and 96 products under investigation, respectively.
- Current marketed products for Alzheimer's disease are focused on symptom management, with recent exceptions including aducanumab and lecanemab; however, most of the products under clinical development are disease modifying.
- Depression and other mental health conditions have become more prevalent and recognized, particularly during the pandemic[1], and account for an increasing amount of the neurology pipeline, with 84 products under development for depression and 31 for anxiety.
- Other rare neurological diseases, such as amyotrophic lateral sclerosis (ALS) and Duchenne muscular dystrophy, continue to receive attention in the pipeline, with promising therapies in development.
- Currently, 72% of the neurology pipeline consists of small molecule products, indicating their continued utility in a rapidly evolving space.
- Next-generation biotherapeutics, such as cell and gene therapies, are increasingly being investigated for neurologic conditions, comprising 11% of the pipeline. These products could show the most promise for treating some of these debilitating diseases.

Notes: Analysis includes products in active research with a focus on neurology therapies. Products being investigated for more than one indication may be included in more than one disease area. Therapy types are non-overlapping and macromolecules (biologics) are those biologic products that are not otherwise noted. Percentages may not sum to 100% due to rounding.

38% of development for rare diseases outside of oncology is focused on gastrointestinal and neurologic diseases

Exhibit 12: Rare disease pipeline excluding oncology, by phase and therapeutic drug class



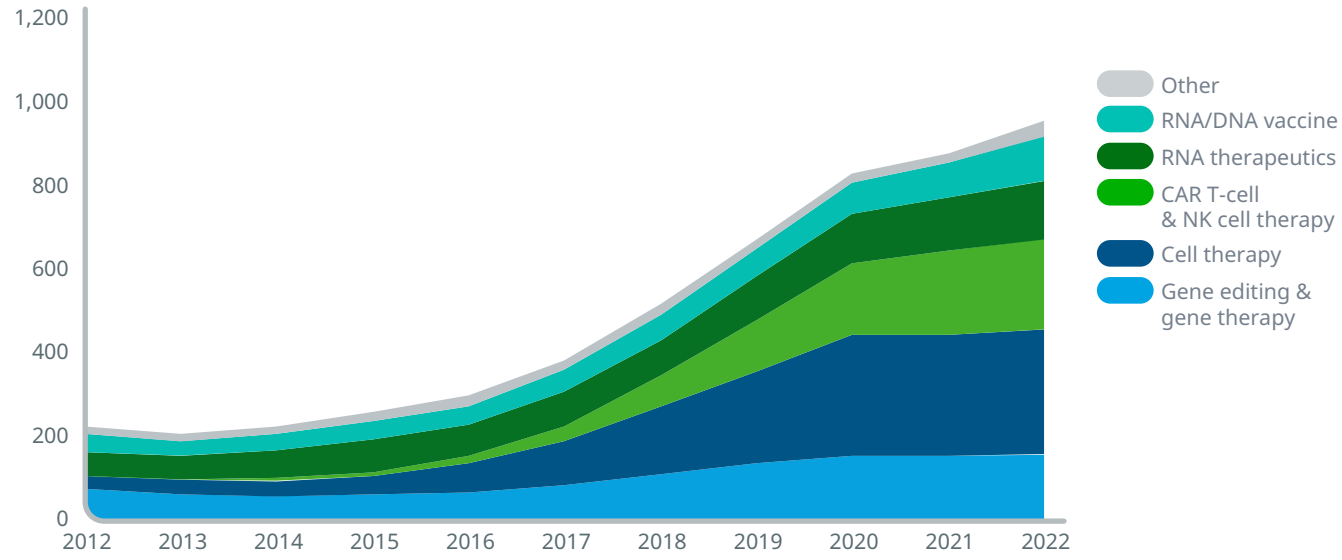
Source: IQVIA Pipeline Intelligence, Dec 2022; IQVIA Institute, Jan 2023.

- Currently, there are 1,824 products (30% of pipeline) under development for rare diseases, with half of these for diseases outside of oncology.
- Phase II makes up a significant portion of the pipeline, reflective of significant numbers of hybrid Phase I/II trials underway with difficult to identify patients, extending their trial durations and contributing to potentially different clinical development journeys for these products.
- Products in development for rare neurological disorders represent the largest share of the rare disease pipeline after rare oncology, accounting for 22%; however, this share declines in later phases and has remained stable over time, indicating difficulties in achieving success in earlier phases for these products.
- Across phases, drug development for rare gastrointestinal conditions has been increasing now accounting for 16% of rare drug development. Nearly half of the rare gastrointestinal pipeline is for treating inherited rare disorders such as lysosomal storage disorders, mucopolysaccharidosis, and Pompe disease, with a high number of gene therapies and other next-generation biotherapeutics to address the underlying genetic modifications for these disorders.

Notes: Includes drugs with an active research program, with phase determined by the highest phase of research regardless of indication. Many drugs have ongoing research for multiple indications, and drugs which have any trials focused on rare diseases have been included as rare. Analysis excludes oncology.

The next-generation biotherapeutic pipeline is focused on gene editing, CAR T-cell and other cell therapies

Exhibit 13: Next-generation biotherapeutics Phase I to regulatory submission pipeline by mechanism, 2012–2022



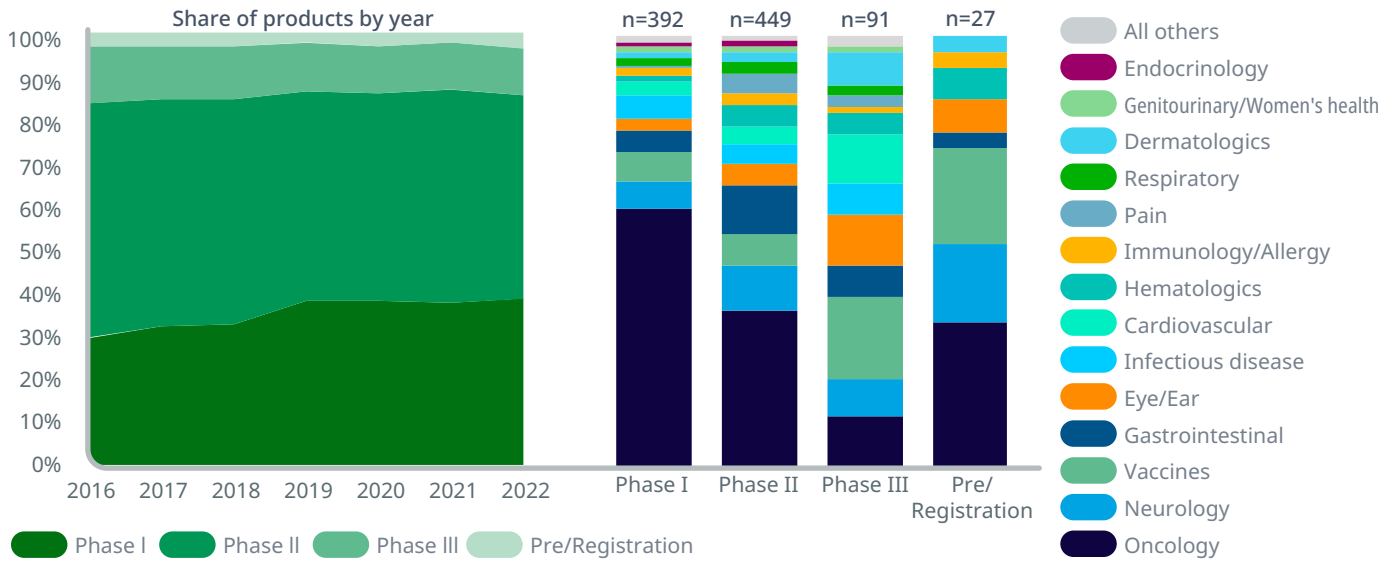
Source: IQVIA Pipeline Intelligence, Dec 2022; IQVIA Institute, Jan 2023.

- In 2022, 960 next-generation biotherapeutics were in development from Phase I through filing with a regulatory agency. The next-generation biotherapeutic pipeline has grown significantly in recent years, with a 20% CAGR since 2017.
- Cell therapies represent the largest share of the next-generation biotherapeutic pipeline with 40% of these being investigated for a range of cancers, predominantly non-rare solid tumor malignancies.
- Gene therapies, including gene editing technologies such as CRISPR, have had moderate growth in recent years following a period of deceleration in the early-2010s. 26% of these are focused on gastrointestinal conditions and eye and ear conditions representing another 16%.
- Even though they were not in development prior to 2012, there are now 217 chimeric antigen receptor T-cell (CAR T-cell) and natural killer (NK) cell therapies in development, representing the second highest share of the next-generation biotherapeutic pipeline, with nearly all in development for cancer.
- RNA-based therapeutics, including RNA interference (RNAi) — the inhibition of expression of certain genes by mRNA — continue to represent a small share of the next-generation biotherapeutic pipeline.
- RNA and DNA vaccines have become increasingly investigated since the COVID-19 pandemic across a range of cancers and infectious diseases (Exhibit 21).

Notes: Includes drugs with an active research program, with phase determined by the highest phase of research regardless of indication. Other includes oligonucleotides and other less common next-generation biotherapeutics.

More than 40% of next-generation biotherapeutics in development in 2022 were for oncology and in earlier stages

Exhibit 14: Next-generation biotherapeutic products pipeline by phase and therapeutic drug class



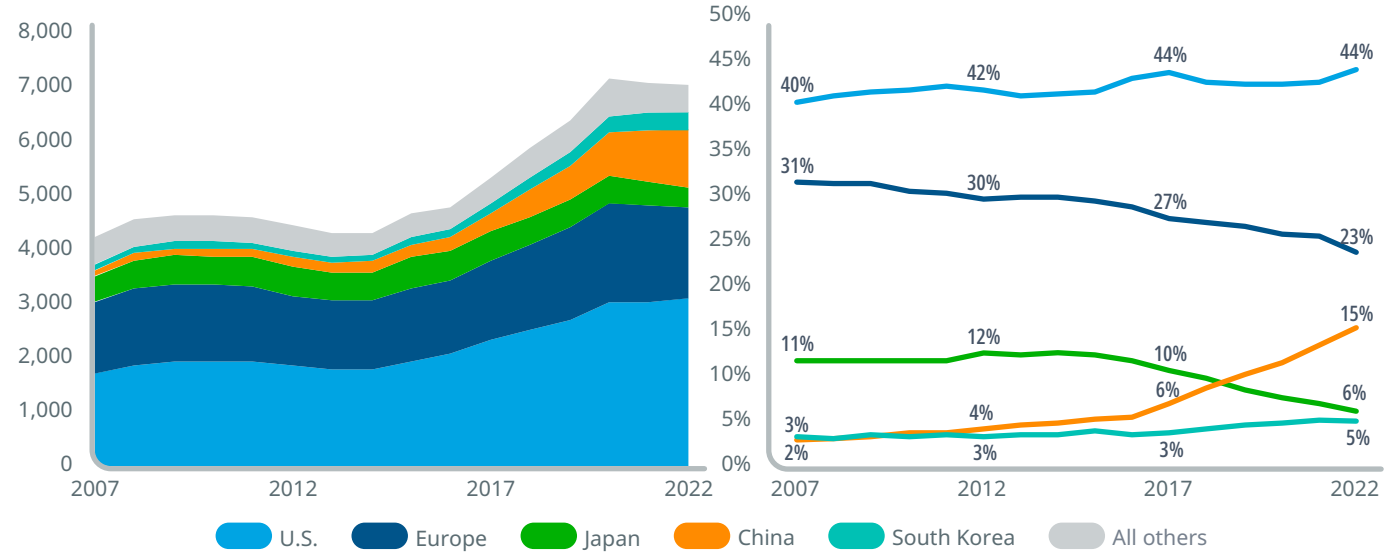
Source: IQVIA Pipeline Intelligence, Dec 2022; IQVIA Institute, Jan 2023.

- More than 85% of the next-generation biotherapeutic pipeline is in Phase I or II, with smaller portions in Phase III and submitted for regulatory review, highlighting the challenges of getting these products to the market.
- Next-generation are defined as cell therapies, gene therapies, gene editing, nucleotide and RNA interference, mRNA therapies and RNA or DNA vaccines.
- Oncology continues to comprise the bulk of next-generation biotherapeutic development (42%), however other disease areas, such as gastrointestinal conditions and neurological disorders, continue to see increasing activity.
- Next-generation vaccines have seen a substantial increase in the last two years, driven by the pandemic's acceleration of mRNA and DNA vaccine technology development. Although COVID-19 remains the focus of these nucleic acid vaccines, these are now being tested for other diseases (Exhibit 21).

Notes: Includes drugs with an active research program, with phase determined by the highest phase of research regardless of indication.

Drugs from China-headquartered companies have risen to 15% of the pipeline from 4% a decade ago

Exhibit 15: Number of drugs over time and country share of pipeline Phase I to regulatory submission based on company headquarters location, 2007–2022



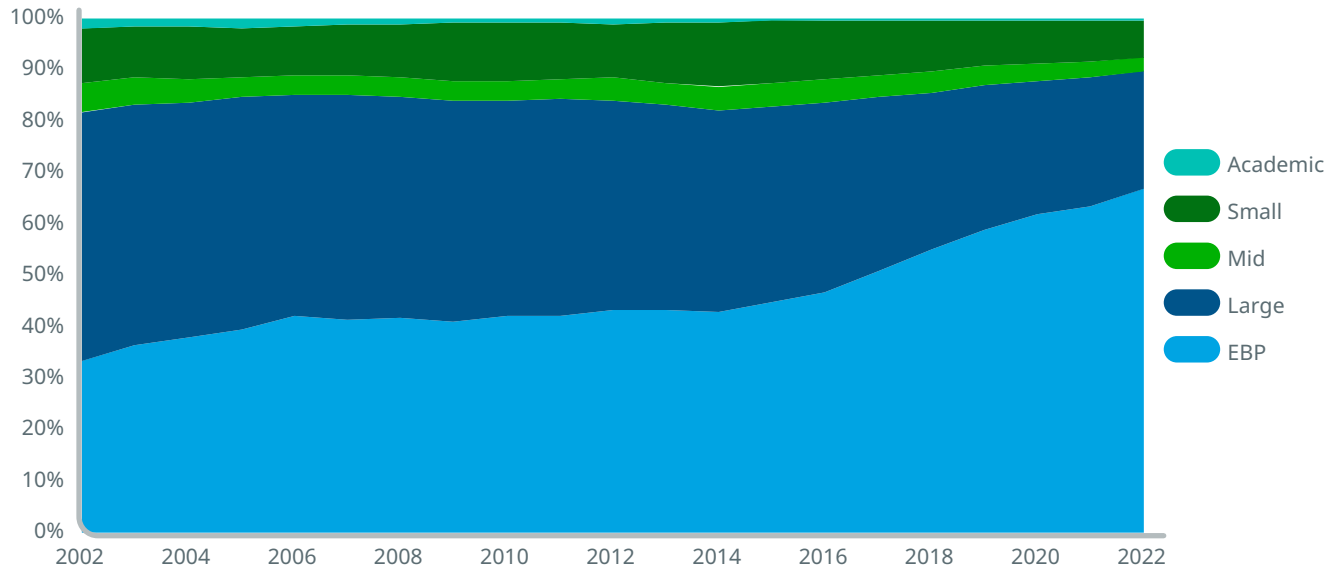
Source: IQVIA Pipeline Intelligence, Dec 2022; IQVIA Institute, Jan 2023.

- Currently, more than 2,700 companies and more than 100 academic or research groups around the world are involved in the R&D pipeline.
- The U.S. share of the global R&D pipeline has remained relatively stable, at above 40% over the past 15 years.
- Europe's share has declined from 31% to 23% over the past 15 years, while the absolute number of active programs grew by 25% — from 1,327 to 1,655.
- Companies headquartered in Japan have seen a declining share of the pipeline, dropping to 6% in 2022, down from 10% five years ago, and a 26% drop in absolute number of active programs since 2017.
- Products from China-headquartered companies now represent 15% of the R&D pipeline, up from 6% five years ago and 2% in 2007. The active pipeline from China-headquartered companies has more than tripled in the last five years, reflecting recent significant investments made in the life sciences there.
- South Korea's share of the pipeline has remained relatively stable despite 92% growth in the absolute number of active programs over the last five years.

Notes: Includes drugs with an active research program, with phase determined by the highest phase of research in each year regardless of indication. Each company involved in a drug's development is counted individually, so products with more than one company involved are counted more than once and may be included in more than one region. Europe is defined as any country in continental Europe.

Emerging biopharma companies are responsible for two-thirds of the R&D pipeline, with their share continuing to grow

Exhibit 16: Share of Phase I to regulatory submission pipeline by company segment, 2002–2022



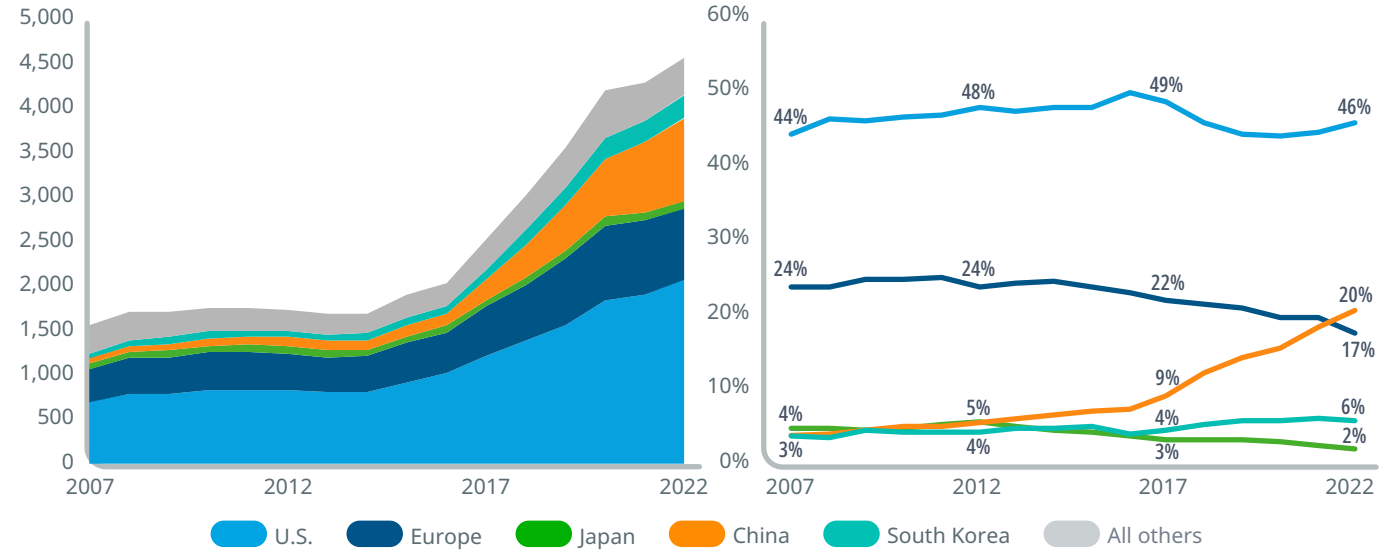
Source: IQVIA Pipeline Intelligence, Dec 2022; IQVIA Institute, Jan 2023.

- The contribution of emerging biopharma companies — those with less than $500Mn in annual sales and R&D spending less than $200Mn per year — continues to increase, while large pharma companies — those with greater than $10Bn in annual sales — represent an increasingly smaller share of the R&D pipeline.
- While emerging biopharma companies were responsible for only one-third of innovation in 2002, they now are responsible for two-thirds of the R&D pipeline, highlighting the increasing importance of innovation from these smaller companies.
- While the number of larger companies actively involved in the R&D pipeline has remained stable since 2017, the number of emerging biopharma companies has grown 26%.
- Large pharma companies now represent just 23% of pipeline activity, down from 48% in 2002, while the absolute number of actively researched drugs rose from 956 to 1,090 for companies of this size.
- Although a small contributor to the clinical pipeline (<1%), academic and research groups play an important role in the R&D pipeline, particularly in advancing work in discovery and pre-clinical phases prior to clinical investigation.

Notes: Includes drugs with an active research program, with phase determined by the highest phase of research regardless of indication. Company segment when two or more companies are involved is determined by the larger sales segment.

Emerging biopharma drug development is rising rapidly, particularly in China, whose share now exceeds that of Europe

Exhibit 17: Number of drugs and country share of emerging biopharma pipeline Phase I to regulatory submission based on company headquarter location, 2007–2022



Source: IQVIA Pipeline Intelligence, Dec 2022; IQVIA Institute, Jan 2023.

- Emerging biopharma company R&D activity is spread out across major geographies, with more than 4,500 products under development by emerging biopharma companies.
- The emerging biopharma pipeline grew 7% in 2022, following a slight plateau in 2021 due to the pandemic, bringing total growth since 2017 to 82%.
- China-headquartered companies now represent 20% of the global emerging biopharma pipeline, up from 9% just five years ago and higher than China's share of the overall pipeline. Growth in the emerging biopharma pipeline was strongest in China compared to other geographies, with 19% growth in the past year.
- The U.S. continues to represent nearly half of the emerging biopharma pipeline, although this share has declined slightly in recent years from a peak of 50% in 2016 to 46% in 2022.
- Europe and Japan represent smaller shares of the emerging biopharma pipeline than they do the overall pipeline, with shares declining since 2012 as innovation has increased in China and South Korea. Europe and Japan saw declines of 5% and 20%, respectively, in the emerging biopharma pipeline over the last year.

Notes: Includes drugs with an active research program, with phase determined by the highest phase of research in each year regardless of indication. Company segment when two or more companies are involved is determined by the larger sales segment. Each company involved in a drug's development is counted individually, so products with more than one company involved are counted more than once and may be included in more than one region. Europe is defined as any country in continental Europe.

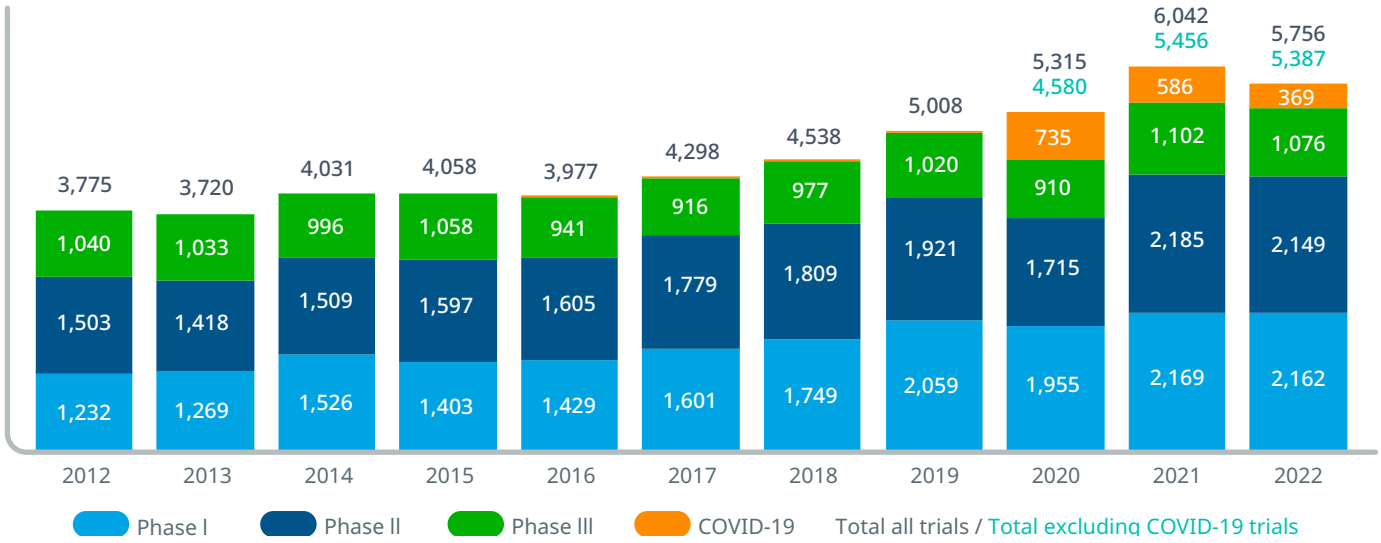
Clinical trial activity

- Clinical trial activity was remarkably resilient even as the pandemic stretched through 2022, with a 2% decline in non-COVID trial activity over 2021, but a restoration of pre-pandemic growth rates with an 8% increase over 2019.
- COVID-19 trials drove recent growth in infectious disease trials, with non-COVID-19 activity focused on a variety of other diseases.
- The total number of clinical trial subjects dropped to 1.8 million in 2022 due to a decline in COVID-19 enrollment.
- The development of mRNA vaccines has accelerated in the last two years and expanded to multiple disease areas beyond COVID-19.
- Oncology trial starts reached historically high levels in 2022, up 22% from 2018 and primarily focused on rare cancer indications.
- Clinical trial starts in other important disease areas returned to pre-pandemic level in 2022.
- Depression trial starts are 68% higher than pre-pandemic, with psychedelics being tested in nearly 25% of 2022 trial starts.
- Black/African American and Hispanic patient clinical trial representation has dropped over the past decade even as it varies widely across therapeutic areas.

Clinical trial activity was remarkably resilient even as the pandemic stretched through 2022, with a 2% decline in non-COVID trial activity over 2021, but a restoration of pre-pandemic growth rates with an 8% increase over 2019.

Total non-COVID-19 clinical trial starts decreased by 2% in 2022, while still 8% above the 2019 level

Exhibit 18: Total number of clinical trial starts by phase, 2012–2022



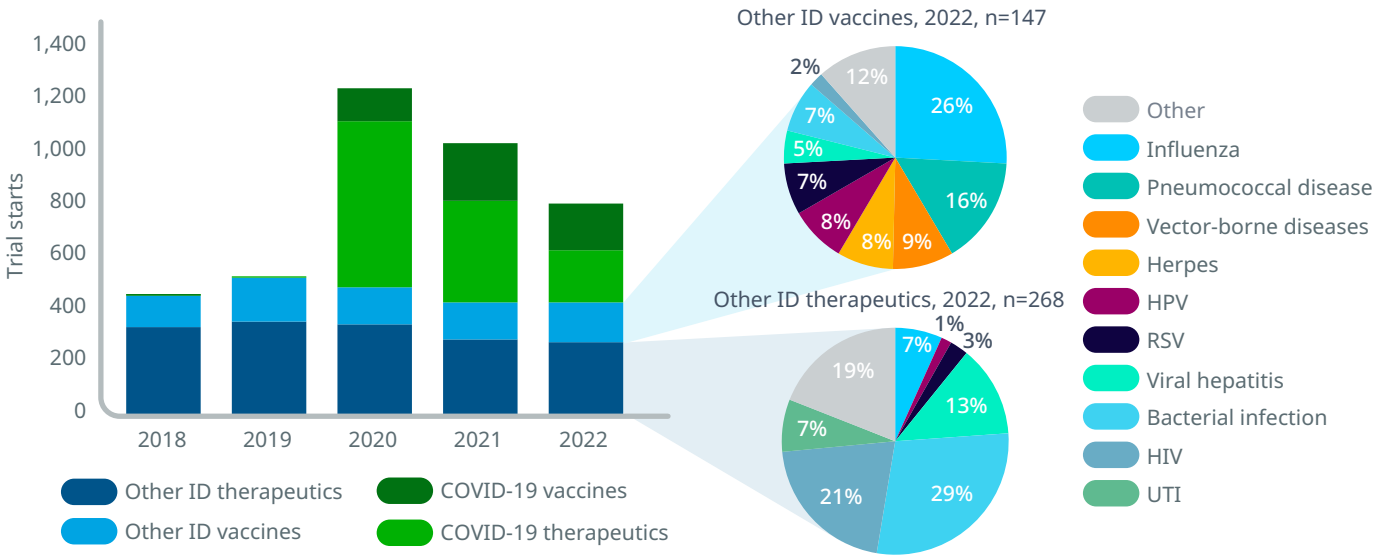
Source: Citeline Trialtrove, Jan 2023.

- Clinical trial activity was remarkably resilient even as the pandemic stretched through 2022, with a 2% decline in non-COVID trial activity over 2021, but a restoration of pre-pandemic growth rates with an 8% increase over 2019.
- COVID-19 trial starts accounted for 10% and 6% of the total in 2021 and 2022 respectively.
- Planned non-COVID-19 Phase II and III trials declined by 2% from 2021, and Phase I declined by 1% while still exceeding pre-pandemic levels of trial starts.
- The double digit increases in planned trial starts in 2021 were related to 2020 trial delays driven by COVID-19 disruptions, and while activity has returned to a more normal trend, not all planned trials reported for 2021 will have started by the end of the year and, accordingly, trial start trends in recent years should be interpreted with caution.

Notes: Phase II includes Phases I/II, II, IIa, IIb. Phase III includes Phase II/III and III. Terminated trials are included to track the activity still involved with their initiation, partial execution and termination. Trials were industry sponsored, interventional trials and device trials were excluded.

COVID-19 trials drove recent growth in infectious disease trials, with non-COVID-19 activity focused on a variety of other diseases

Exhibit 19: Infectious disease clinical trial starts by disease



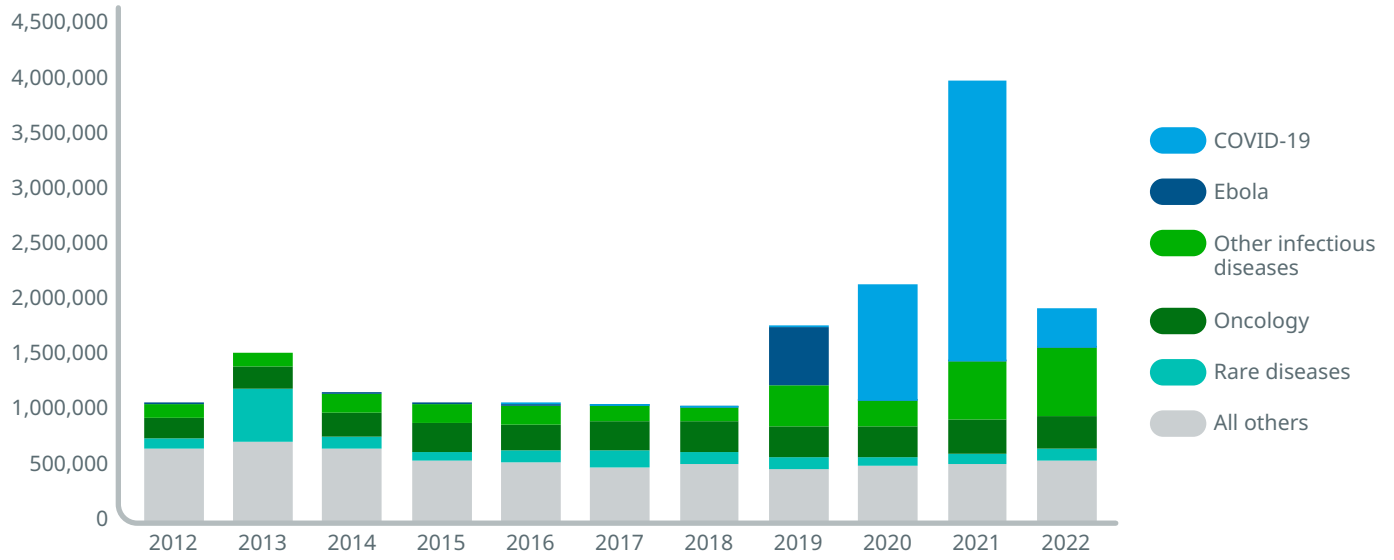
Source: Citeline Trialtrove, IQVIA Institute, Jan 2023.

- Infectious disease trials showed a dip in non-COVID-19 starts in early 2020, concurrent with the appearance of the first COVID-19 trials.
- By mid-2020, a surge in trial starts had COVID-19-related trials nearly tripling those of infectious disease trial starts.
- New COVID-19 trials have dropped to less than half the level in 2020 as fewer new targets have een identified.
- Overall, non-COVID-19 infectious disease trial activity has focused on therapeutics to a greater degree than vaccines.
- While there has been some overlap in the areas of focus, the relative priority for vaccines has remained on flu and pneumococcal trials, while therapeutics have focused on bacterial infections, HIV and hepatitis.
- Bacterial infections represent 21% of infectious disease trial starts in the last year, notable considering the continued lack of novel mechanisms and targets and the growing risks of antimicrobial resistance.

Notes: Includes Phase I, Phase II (Phases I/II, II, IIa, IIb) and Phase III (Phase II/III and III). Terminated trials are included to track the activity still involved with their initiation, partial execution and termination. Trials were industry sponsored, interventional trials.

The total number of clinical trial subjects dropped to 1.8 million in 2022 due to decline in COVID-19 enrollment

Exhibit 20: Clinical trial subjects, all phases, all diseases, 2012–2022



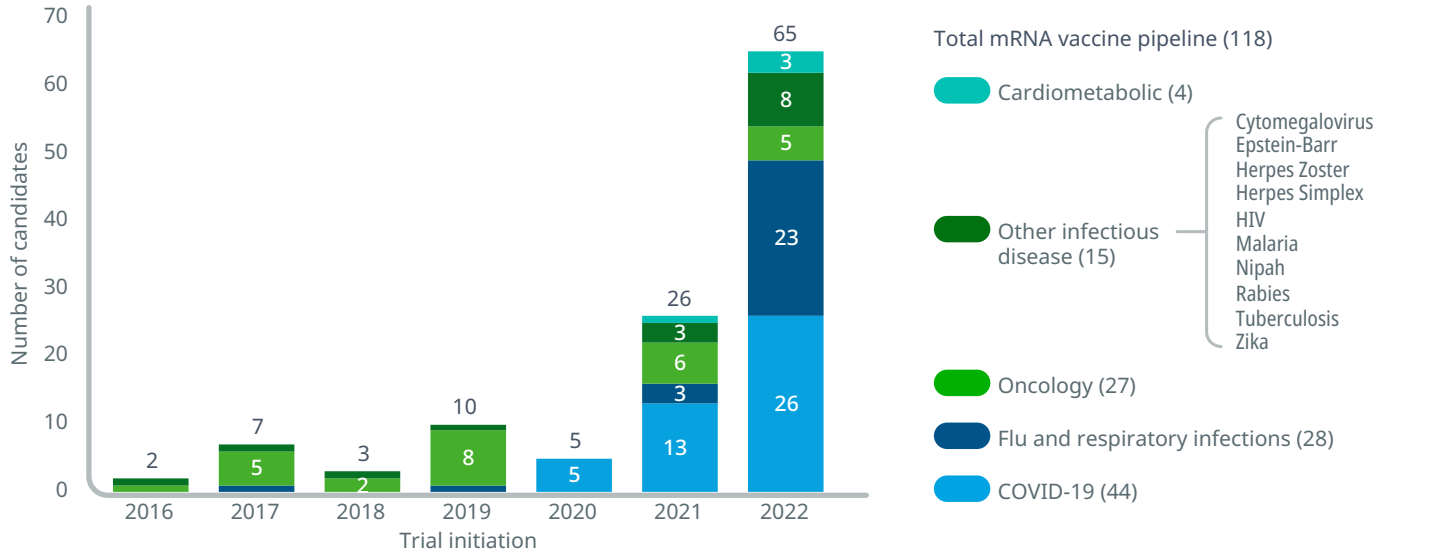
Source: Citeline Trialtrove, IQVIA Institute, Jan 2023.

- The last four years have seen record-breaking numbers of subjects planned or enrolled in clinical trials, with the number approaching 4 million in 2021, and still an exceptional 1.9 million in 2022.
- The largest area of increase in study subjects has been infectious diseases, and even excluding COVID-19 and Ebola, other infectious diseases had nearly 600,000 subjects in 2022 compared to 125,000 in 2018.
- In addition to the 1 million COVID-19 subjects in 2020, studies enrolled another 2.4 million in 2021 and more than 330,000 in 2022.
- Oncology trials accounted for 16% of the industry's clinical trial subjects in 2022, with 289,000 subjects, down by 9,000 subjects but up from 8% of all trial subjects in 2021.
- As the COVID-19 vaccine trial surge recedes, the industry has an opportunity to keep the large set of recent trial subjects engaged for participation in ongoing and future clinical research.
- The number of subjects in trials is generally trending down as more trials focus on niche populations, although this has been reversed with some large population trials for infectious diseases, as well as cardiovascular and other metabolic trials (Exhibit 39).

Notes: Subjects are the reported target or actual patients reported for trials with planned or actual start dates in each year.

The development of mRNA vaccines has accelerated in the last two years and expanded to multiple disease areas

Exhibit 21: mRNA vaccine pipeline by therapy area, 2016–2022



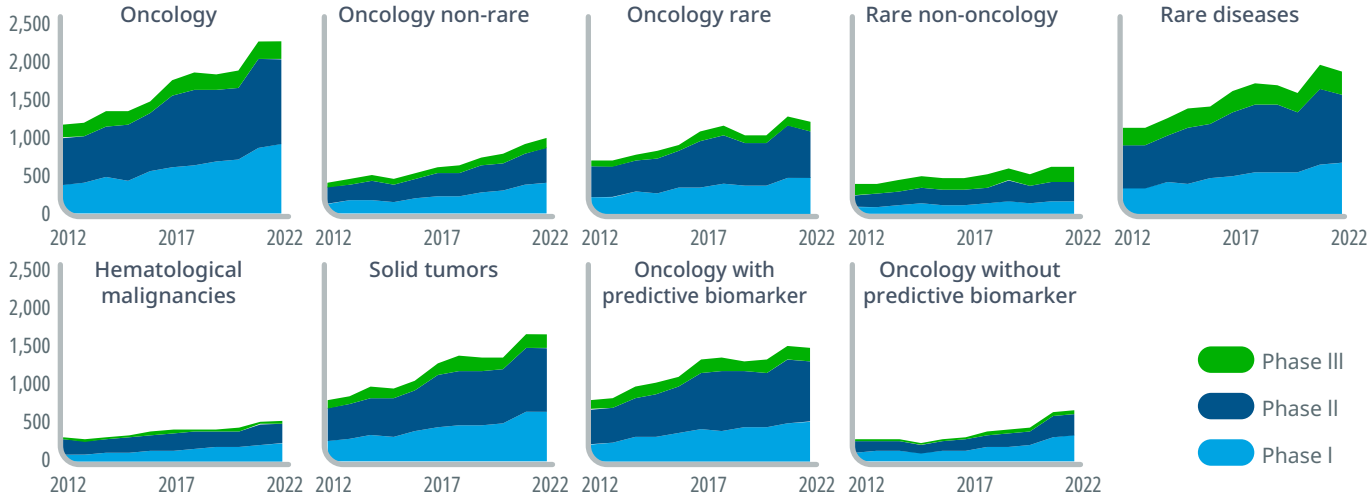
Source: IQVIA Institute, Jan 2023.

- Clinical testing of mRNA vaccines has dramatically increased since 2016 with a more than 30-fold increase in the number of candidates by 2022.
- Starting in 2020, COVID-19 mRNA vaccines accounted for a significant portion of this growth and increased from 5 candidates beginning in 2020 to 26 in 2022.
- The increased focus on mRNA vaccines as a result of COVID-19 vaccine development seems to have boosted other development with non-COVID-19 mRNA candidate development increasing 12-fold in the last five years.
- mRNA vaccine development for flu and respiratory infections was the highest non-COVID-19 segment in 2022, representing 35% of the development activity.
- Despite making up the largest proportion of the pre-COVID-19 mRNA pipeline, oncology focused mRNA vaccines have not drastically increased and make up 8% of the pipeline in 2022.

Notes: Chart shows number of mRNA vaccine candidates under clinical development arranged based on the earliest trial start date.

Oncology trial starts remained at historically high levels in 2022, up 22% from 2018 and primarily focused on rare cancer indications

Exhibit 22: Clinical trial starts by year, 2012–2022



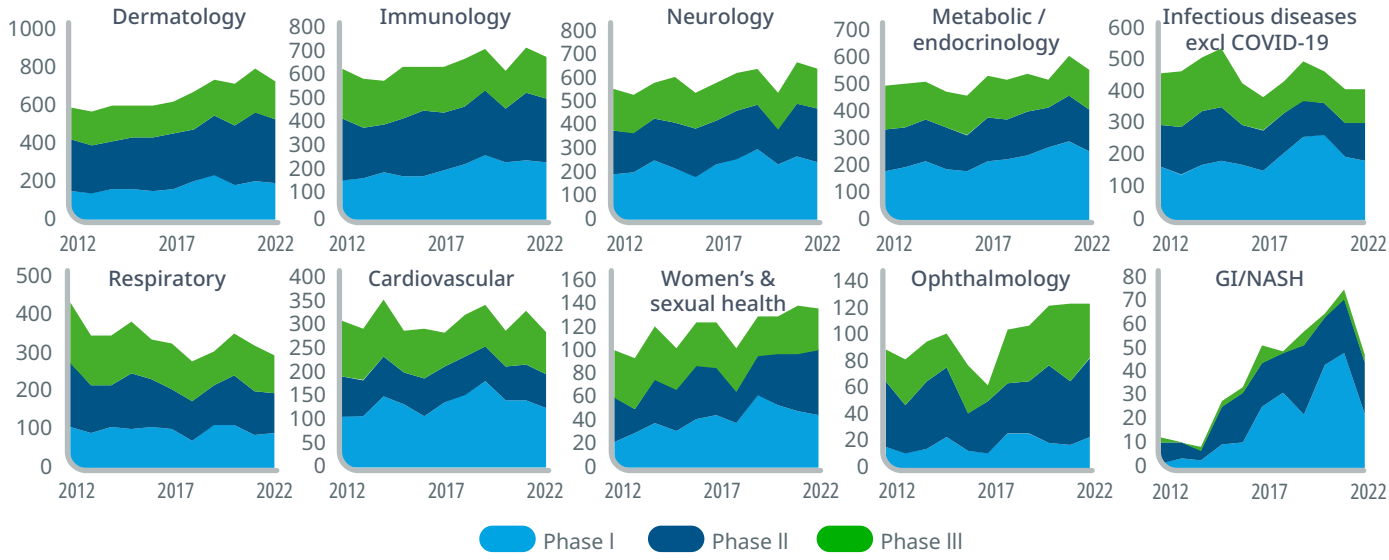
Source: Citeline Trialtrove, IQVIA Institute, Jan 2023.

- Oncology and rare disease remain the two most active, though overlapping, therapeutic areas for trial starts in 2022, making up 40% and 33% of trial starts respectively in 2022.
- Though both areas have shown steady increases in trial starts for most of the past decade, rare disease and oncology rare both show a dip in 2022 as a function of their heavy overlap.
- Within oncology, rare disease starts have been variably up and down in the past four years, while non-rare oncology has been consistently growing - oncology non-rare represented 44% of the oncology trial starts in 2022, which is the highest relative level in at least the past 10 years.
- The number of solid tumor trial starts has been growing steeply across the decade, although they remained stable in 2022; hematological trial starts have grown more slowly over the past 10 years.
- Predictive biomarker use has been increasing steadily over the past 10 years as well, and now includes at least three-quarters of the oncology pipeline, and much like the rest of the oncology pipeline, saw no growth in 2022.

Notes: Phase II includes Phases I/II, II, IIa, IIb. Phase III includes Phase II/III and III. Terminated trials are included to track the activity still involved with their initiation, partial execution and termination. Trials were industry sponsored, interventional trials and device trials were excluded. Oncology has been segmented into hematological or solid tumor in two charts, and into those with predictive biomarker and without biomarkers in two charts. Each pair of charts totals overall oncology.

Clinical trial starts in other important disease areas returned to pre-pandemic levels in 2022

Exhibit 23: Industry sponsored interventional trials by start date, 2012–2022



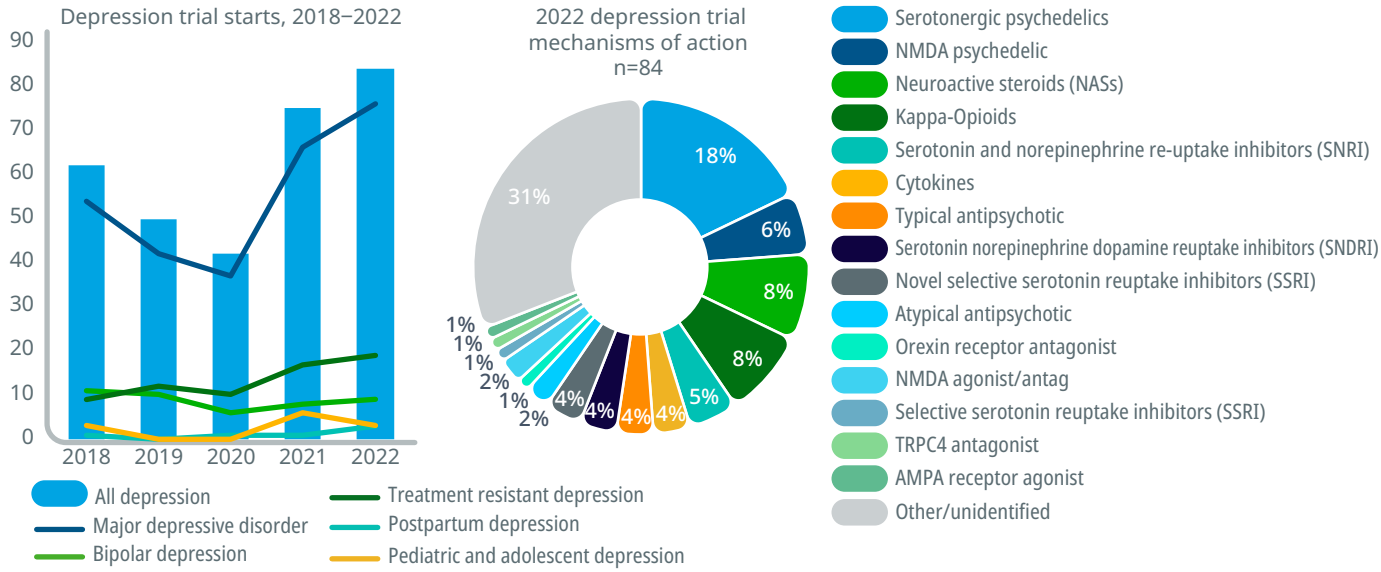
Source: Citeline Trialtrove, IQVIA Institute, Jan 2023.

- Many of the key non-oncology therapeutic areas showed a very slight decrease in clinical trial starts in 2022 versus 2019, but in many cases, still remained above 2020 levels, suggesting a return to pre-pandemic growth patterns.
- Exceptions to this include ophthalmology, infectious disease and women's health, where trial starts matched or slightly exceeded 2021 levels.
- Both NASH and respiratory show a slightly steeper decline, with respiratory continuing a decline started in 2020, and NASH total trial starts dropping by 37% between 2021 and 2022.

Notes: Phase II includes Phases I/II, II, IIa, IIb. Phase III includes Phase II/III and III. Terminated trials are included to track the activity still involved with their initiation, partial execution and termination. Trials were industry sponsored, interventional trials and device trials were excluded.

Depression trial starts were 68% higher in 2022 than pre-pandemic with psychedelics being tested in nearly 25% of the 2022 trial starts

Exhibit 24: Depression clinical trials by segment and mechanism of action



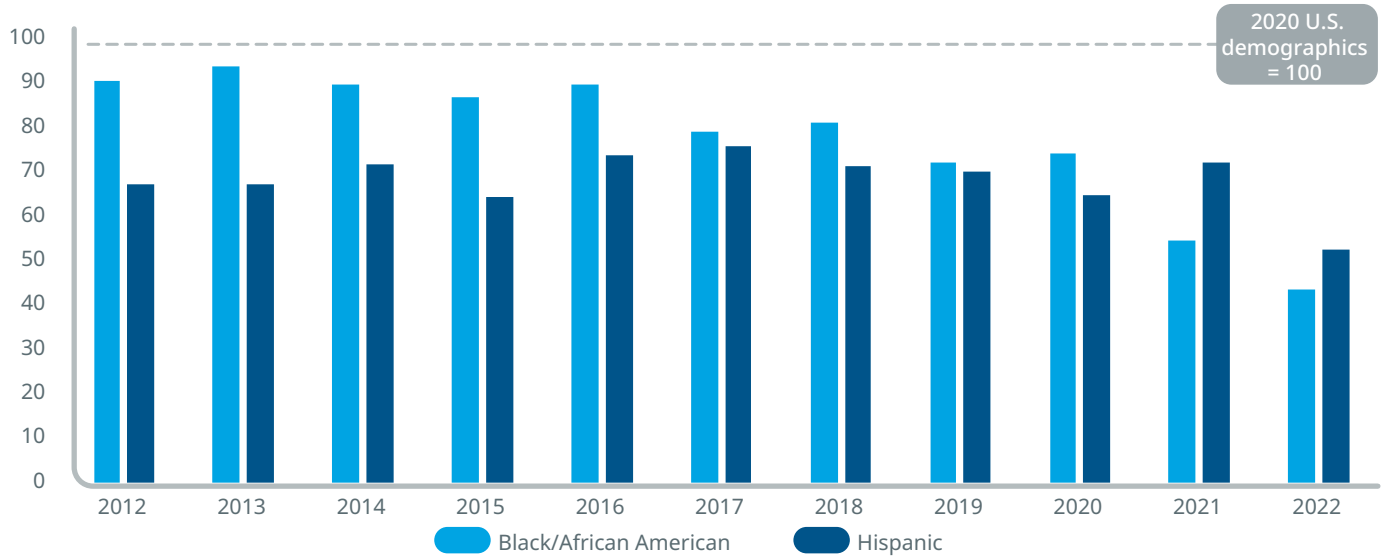
Source: Citeline Trialtrove, IQVIA Institute, Jan 2023.

- Overall depression trial starts have increased by 35% in the past five years and have seen a particularly sharp rise since 2020.
- Major depressive disorder remains the most active segment, with more than 90% of 2022 trial starts.
- Activity around other key depression segments include minor increases in the last three years, but these still account for a small portion of the trial starts in 2022, with treatment resistant depression a focus in 23%, postpartum depression in 3%, and pediatric and adolescent depression in 3% of trial starts.
- In addition to top line segments, depression trials are focused on patients with a broad variety of co-morbidities and depression types (not shown).
- Notably, despite significant publicity, COVID-19 associated depression starts only accounted for 2% of the trial pipeline in 2022.
- As researchers and clinicians navigate a complex matrix of depression phenotypes across patients, the focus on mechanisms of action is becoming more targeted and hypothesis-driven.[2]
- Analysis of depression drug mechanisms of action paints a very complex picture with a variety of emerging novel mechanisms entering clinical testing, including novel serotonin reuptake inhibitors, neurotropic steroids, serotonergic psychedelics and NMDA psychedelics, which together account for 36% of the 2022 trial pipeline.
- Despite psychedelics now representing 24% of the trial starts in 2022, their potential role is evolving as sponsors and regulators will need to negotiate highly intensive regulatory and administration burden and unique uncertainties related to these controlled substances both in later stage clinical trials and in clinical practice.

Notes: Trials may focus on more than one segment and depression segment analysis includes some double counting as a result. Additionally, segment assignment depends on reporting in the data source, and secondary depression segmentation may be under counted in the data set.

Black/African American and Hispanic patient clinical trial representation dropped over the past decade

Exhibit 25: Phase II and III racial and ethnic inclusion indexed to U.S. demographics



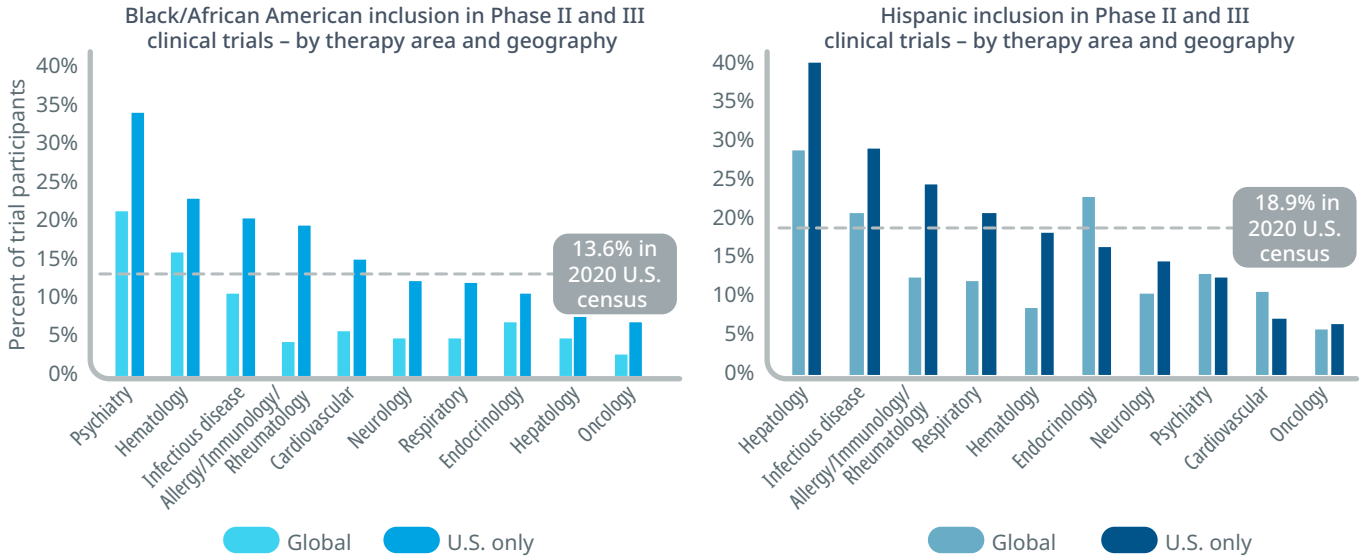
Source: ClinicalTrials.gov, Dec 2022; U.S. Census Bureau QuickFacts, accessed Jan 2023; IQVIA Institute, Jan 2023.

- Despite increasing sponsor focus on diversity in clinical trials and diversity data reporting, and recent FDA guidance on diversity data reporting and clinical program diversity planning, Black/African American and Hispanic patient inclusion failed to reach U.S. demographic levels on average across interventional trials, including U.S. sites in the past decade.[3,4,5]
- Black/African American participation has been declining over the past decade, with an inclusiveness drop most notable in the past five years, with a 46% decline in U.S. Census indexed inclusion between 2018 and 2022 — from 81% of US demographics to 43%.
- Hispanic inclusiveness has varied over the past decade and does not show as distinct a decline as Black/African American inclusion, but also never reached U.S. demographic levels in the past decade. Hispanic patients were enrolled in trials at 53% of U.S. demographic levels in 2022.
- Black/African American and Hispanic patients are critically under-represented in trials using U.S. clinical sites and seeking U.S. regulatory approval and are indicative of broader clinical development diversity opportunities to address ongoing healthcare disparities and expected ongoing regulatory and legislative requirements.[3,4,5]

Notes: Includes all interventional Phase II and III trials with industry involvement and any U.S. sites listed on ClinicalTrials.gov starting after 2009 and completing between the start of 2012 and the end of 2022. Only trials with racial or ethnic data collected were included in calculation of Black/African American or Hispanic patient inclusion, respectively. Analysis includes 4,947 trials over the time period. US average Black / African American representation is 13.6% and Hispanic representation is 18.9%.

Black/African American and Hispanic clinical trial participation varies widely across therapeutic areas in U.S. vs. global trials

Exhibit 26: Phase II and III Black/African American and Hispanic patient inclusion by therapeutic area and geography, 2020–2022



Source: ClinicalTrials.gov, Dec 2022; U.S. Census Bureau QuickFacts, accessed Jan 2023; IQVIA Institute, Jan 2023.

- While Black/African American and Hispanic inclusion varied across therapeutic areas, both were higher across all therapeutic areas in trials which were recruited exclusively in the U.S., and both saw lowest levels of inclusion in oncology.
- Specifically, Black/African American inclusion in therapeutic and geographic subsets ranged from 34% (2.5 times higher than U.S. demographic) of patients in U.S.-site-only psychiatry trials run between 2020 and 2022 to 3% (20% of the U.S. demographic levels) of globally run oncology trials in the same time period.
- Similarly, Hispanic inclusion ranged from 44% (2.3 times higher than the U.S. Hispanic demographic) in U.S. run hepatology studies to 6% (31% of U.S. demographic) of globally run oncology trials.
- Notably, even in U.S.-site-only trials, Black/African American and Hispanic inclusion in oncology only reached 51% and 35% of the U.S. demographic levels respectively.
- Given the significant proportion of the industry trial pipeline made up by oncology, averaging 38% over the past five years, the impact of poor inclusivity in oncology trials is driving the industry average inclusivity down across the timeframe.
- The dramatic inclusivity disparities in the largest clinical development segment mirrors some of the starkest healthcare disparities in the U.S. and provides directed improvement opportunities that can impact the entire pipeline and healthcare outcomes at large.[6,7]

Notes: Includes all interventional Phase II and III trials with industry involvement and any U.S. sites listed on ClinicalTrials.gov starting after 2009 and completing between the start of 2020 and the end of 2022. Only trials with racial or ethnic data collected were included in calculation of Black/African American or Hispanic patient inclusion, respectively.

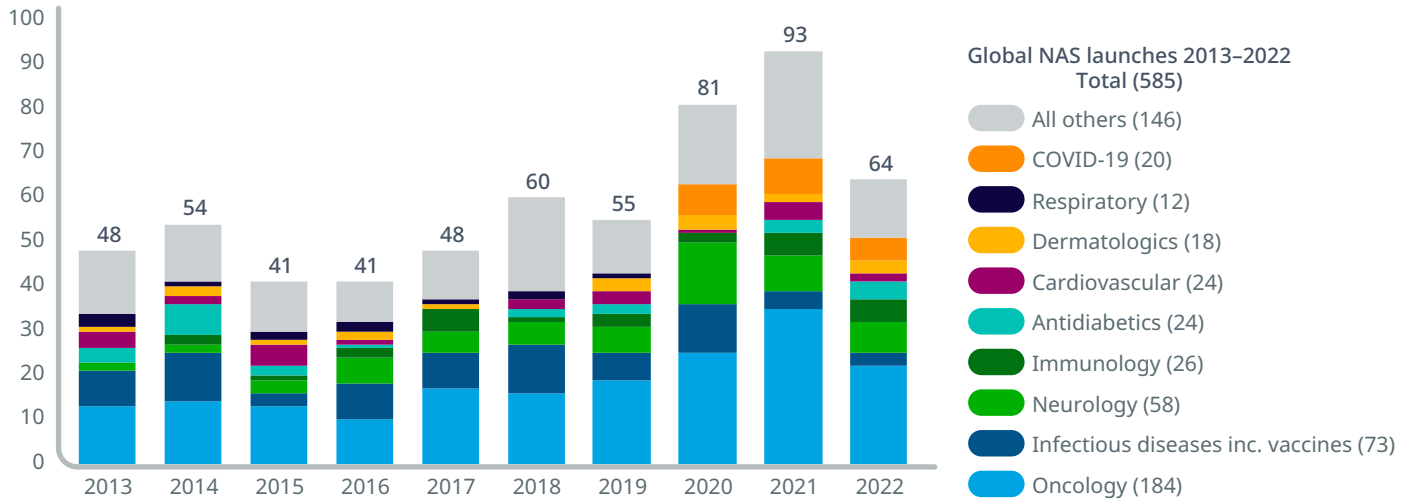
New drug approvals and launches

- A total 64 novel active substances (NASs) launched globally in 2022, a decline from the more than 80 launched in each of the prior two years but representing a return to pre-COVID-19 levels of NAS launches.
- Declines in global NAS launches in 2022 were driven by fewer COVID-19 vaccines and therapeutics as the pandemic's effects on society lessened, there were fewer U.S. accelerated approvals, and fewer NASs were launched only in China.
- A growing share of new launches in 2022 were first-in-class, reflecting the increasing availability of novel science for patients. Additionally, new launches are increasingly specialty products due to the growing number of complex molecules launched that often require advanced distribution and management systems to deliver them to patients.
- Since the first next-generation biotherapeutic launched in 1998, 42 next-generation biotherapeutics — including cell, gene and RNA therapies — have launched globally, with 19 occurring in the last three years and six of the 39 U.S. NAS launches in 2022, including two cell therapies, two gene therapies, and two RNAi therapies.
- Emerging biopharma companies originated 67% of all new drugs in 2022 and launched 69% of those, indicating more independence on the part of EBP companies in taking products from innovation to market.
- A total of 353 novel active substances have launched globally in the past five years, bringing the 20-year total to 903, with variations in timing of launch and access to these medicines across major geographies.

The number of global novel actives substances launched dropped by nearly a third in 2022 but still exceeded all pre-COVID-19 years and included a higher percentage of first-in-class drugs driving increased availability of novel science for patients.

A total of 64 novel active substances (NASs) were launched globally in 2022

Exhibit 27: Global launches of novel active substances (NAS) by therapy area, 2013–2022



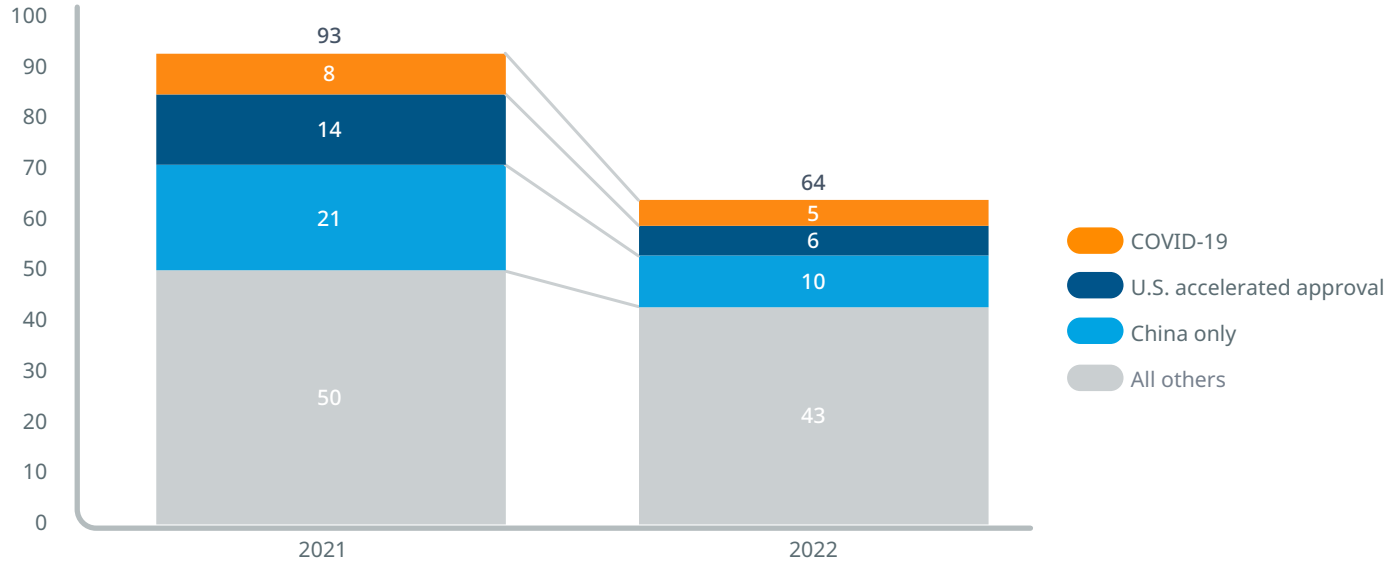
Source: IQVIA Institute, Jan 2023.

- A total 64 novel active substances (NASs) launched globally in 2022, a decline from the more than 80 launched in each of the prior two years but representing a return to pre-COVID-19 levels.
- Oncology, neurology, and immunology have had rising shares of new launches in the past five years, with 173 of the 353 launches (49%) compared to 95 of 232 (41%) from 2013 to 2017.
- Infectious diseases, including COVID-19 as well as anti-bacterial, anti-viral, anti-fungal and anti-parasitic treatments, have included novel treatments for HIV, Ebola, and more recently monkeypox, and are 16% of NAS launches over the last decade, with some year-to-year variability.
- The total 184 oncology launches in the past decade include some of the most groundbreaking new treatments in immuno-oncology as well as next- generation biotherapeutics, and many treatments for rare cancers.
- Neurology includes 58 drugs in 10 years, and many of the more recent launches are for rare neuromuscular diseases as well as the new CGRP mechanism for migraine treatment, the first new mechanism for migraines in decades.
- The first next-generation biotherapeutic, an antisense oligonucleotide to treat cytomegalovirus retinitis, was launched globally in 1998. Since then, 42 next-generation biotherapeutics — including cell, gene and RNA therapies — have launched globally, with 19 occurring in the last three years.

Notes: A novel active substance (NAS) is a new molecular or biologic entity or combination where at least one element is new. Includes NASs launched anywhere in the world by year of first global launch. Launch is determined using IQVIA audits of sales activity as well as companies' public statements. Oncology includes supportive care & diagnostics. COVID-19 includes novel medicines only, and does not include previously approved medicines with new approved uses for COVID-19.

Global NAS launches declined in 2022, driven by declines in COVID-19, China only, and U.S. accelerated approval launches

Exhibit 28: Global launches of novel active substances (NASs) by characteristic, 2021–2022



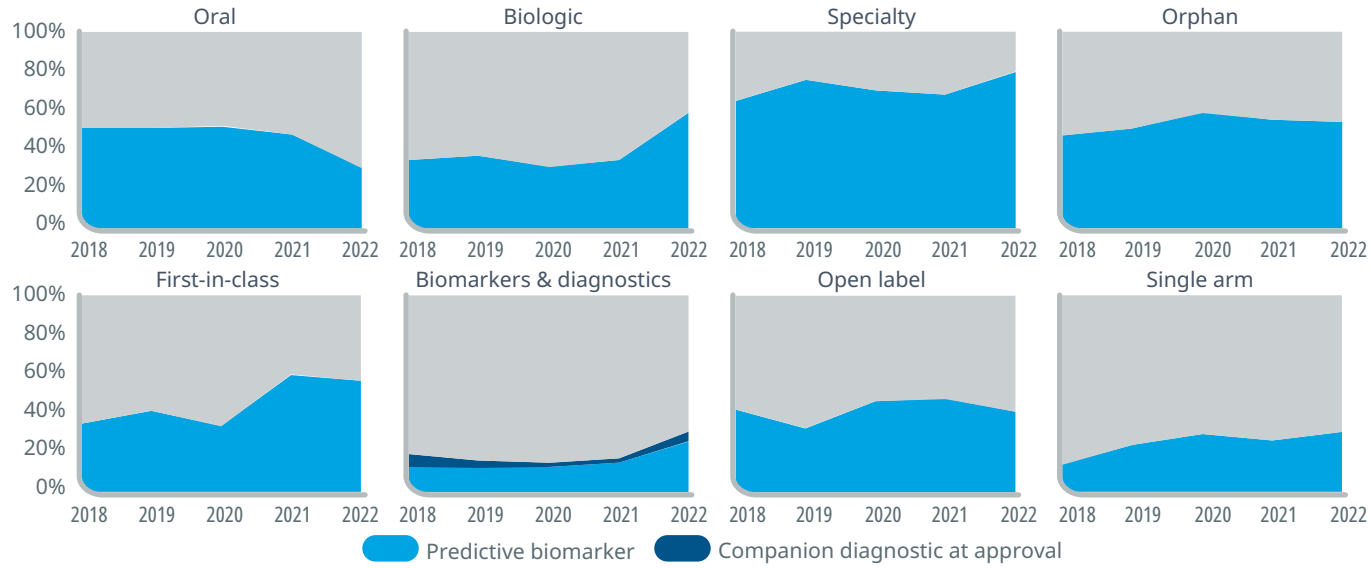
Source: IQVIA Institute, Jan 2023.

- The 64 NASs launched globally in 2022 was a significant drop from the 93 launched globally in 2021, which was a record year and included a variety of unique launches.
- A small drop in the number of NASs can be attributed to a decline in the number of novel COVID-19 therapeutics and vaccines, a result of the declining impact of the pandemic on society and a shift away from COVID-19 pharmaceutical development.
- Across applications for new drugs and biologics and supplemental applications, the U.S. Food and Drug Administration approved 25 through accelerated approvals in 2021 and dropped to less than half that in 2022. Of the global NAS launches between 2021 and 2022, a decline of 8 can be attributed to fewer U.S. accelerated approvals which represents a return to 2019 levels.
- China has seen an increasing number of NASs launched only domestically and not in other major markets. The number of NASs launched in China only had remained low in previous years (5–6) but increased to a peak of 21 in 2021 and fell back to 10 in 2022, more consistent with historic levels.

Notes: Segmentations are non-overlapping and all COVID-19 NAS are grouped regardless of other characteristics. China only NAS are those only launched in China and not in other major markets.

More than 60% of new launches in 2022 were first-in-class and more than half were biologic, up from 35% five years ago

Exhibit 29: U.S. novel active substances (NASs) by product attributes and characteristics of clinical trials used for approval, 2018–2022



Source: IQVIA Institute, Jan 2023.

- Over the past five years, a significant number of first-in-class medicines have become available, rising to 62% of those launched in 2022 and averaging 46% for the last five years.
- Over the past five years, 143 drugs launched with orphan drug designations, representing 53% of the 268 launches, indicating a significant focus of innovative medicines for rare diseases.
- Specialty medicines — those which treat chronic, complex or rare diseases and which also have complex treatment, distribution or patient management aspects, along with often high costs, made up 85% of the launches in the U.S. in 2022 with only six of the 39 2022 launches being traditional medicines.
- Unsurprisingly, this increase in specialty medicines in 2022 coincides with an increase in NAS that are biologics (59%) and a decrease in those that are oral administered (31%), as biologic medications and those provided by injection or infusion frequently result in more complex distribution and patient management as well as higher costs.
- As new medicines have increasingly targeted areas of high unmet need, clinical trial designs have used single-arm and open label designs, common in areas where it is less feasible or practical to conduct a more traditional randomized placebo-controlled trial. Open-label trials were used in the approval trials for 43% of launches over the past five years.

Notes: Includes NASs launched in the United States 2018–2022 regardless of the timing of FDA approval. Orphans include drugs with one or more orphan indications approved by the FDA at product launch. Products are not reclassified as orphan if they subsequently receive an approval for an orphan designated indication. First-in-class is based on FDA classification. Predictive biomarkers and companion diagnostics based on FDA approval information. Open label and single arm are clinical trial attributes determined based on the trial designs of trials noted by FDA as being relevant for the approval.

Novel active substances (NASs) launched in 2022 included 33 specialty drugs and 26 EBP originated

Exhibit 30: Novel active substances (NASs) launched in 2022 in the United States

*ATTRIBUTES KEY: 1 = Oral, 2 = Biologic, 3 = Specialty, 4 = Next-gen biotherapeutic, 5 = Orphan, 6 = First-in-class, 7 = Expedited review, 8 = U.S Patent to launch ≤5 years 9 = EBP originated, 10 = EBP launched

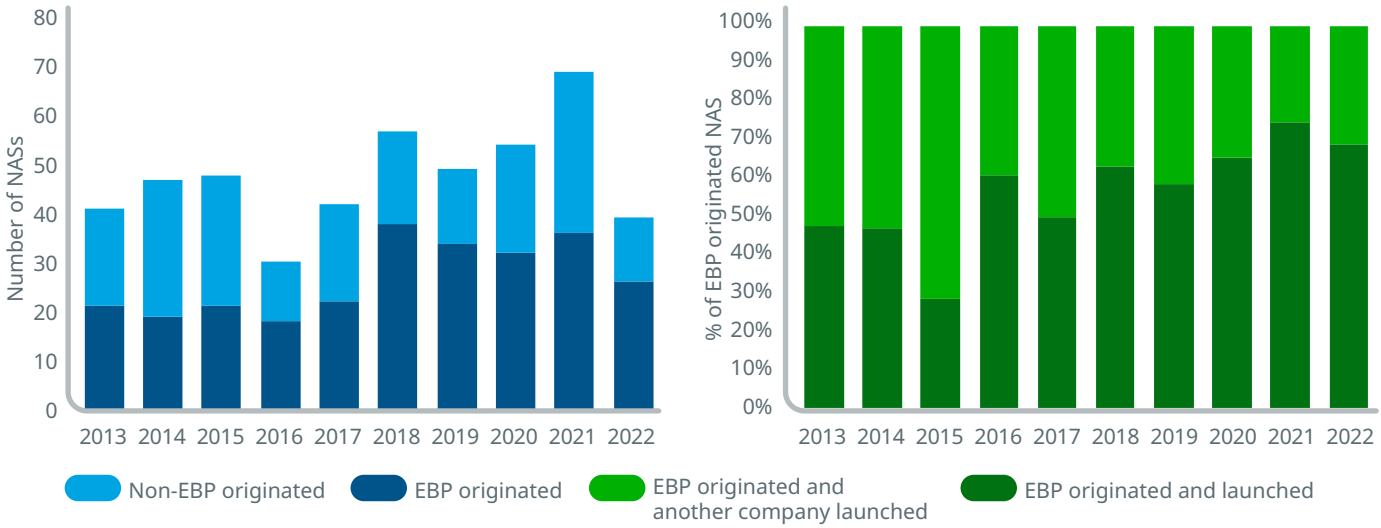
THERAPY AREA	INDICATION	MOLECULE	BRAND	ATTRIBUTES* 1	2	3	4	5	6	7	8	9	10
Oncology	Acute myeloid leukemia	olutasidenib	Rezlidhia	●		●		●			●	●	●
	FRα positive, platinum-resistant epithelial ovarian, fallopian tube, or primary peritoneal cancer	mirvetuximab soravtansine	Elahere		●	●		●	●	●		●	●
	Hepatocellular carcinoma	tremelimumab	Imjudo		●	●		●		●			
	Myelofibrosis	pacritinib	Vonjo	●		●		●		●		●	●
	Neutropenia	eflapegrastim	Rolvedon		●	●							●
	Non-small cell lung cancer (NSCLC)	adagrasib	Krazati	●		●		●		●	●	●	●
	Prostate-specific membrane antigen (PSMA)-positive metastatic castration-resistant prostate cancer (mCRPC)	lutetium (177lu) vipivotide tetraxetan	Pluvicto			●			●	●		●	
	Relapsed or refractory multiple myeloma	ciltacabtagene autoleucel	Carvykti		●	●	●	●		●		●	
		teclistamab	Tecvayli		●	●		●	●	●			
	Unresectable or metastatic melanoma	nivolumab + relatlimab	Opdualag		●	●		●	●	●			
	Unresectable or metastatic uveal melanoma	tebentafusp	Kimmtrak		●	●		●	●	●		●	●
Neurology	Amyotrophic lateral sclerosis (ALS)	sodium phenylbutyrate + taurursodiol	Relyvrio	●		●		●		●		●	●
	Cerebral adrenoleukodystrophy	elivaldogene autotemcel	Skysona		●	●	●	●	●	●		●	●
	Cyclin-dependent kinase-like 5 (CDKL5) deficiency disorder (CDD)	ganaxolone	Ztalmy	●		●		●	●	●		●	●
	Insomnia	daridorexant	Quviviq	●								●	●
	Myasthenia gravis	efgartigimod alfa	Vyvgart		●	●		●	●	●		●	●
	Polyneuropathy of hereditary transthyretin-mediated amyloidosis	vutrisiran	Amvuttra		●	●	●	●		●		●	●
Immunology	Atopic dermatitis	abrocitinib	Cibinqo	●		●				●			
		tralokinumab	Adbry		●	●			●			●	
	Plaque psoriasis	deucravacitinib	Sotyktu	●		●			●				
	Pustular psoriasis	spesolimab	Spevigo		●	●		●	●	●	●		
	Severe asthma	tezepelumab	Tezspire		●	●			●	●			
Hemat-ology	Hemolytic anemia	mitapivat	Pyrukynd	●		●		●	●	●		●	●
	Hemophilia B	etranacogene dezaparvovec	Hemgenix		●	●	●	●	●	●		●	
	Cold agglutinin disease	sutimlimab	Enjaymo		●	●		●	●	●		●	
	β-thalassemia	betibeglogene autotemcel	Zynteglo		●	●	●	●	●	●		●	●
Infectious diseases	COVID-19	bebtelovimab			●	●					●		
	Dengue fever	dengue tetravalent vaccine	Dengvaxia		●					●		●	
	Recurrent vulvovaginal candidiasis (RVVC)	oteseconazole	Vivjoa	●						●		●	●
Anti diabetic	Stage 3 and Stage 2 type 1 diabetes	teplizumab	Tzield		●	●			●	●		●	●
	Type 2 diabetes mellitus	tirzepatide	Mounjaro		●				●	●			
Cardio vascular	Heterozygous familial hypercholesterolemia (HeFH) or atherosclerotic cardiovascular disease (ASCVD)	inclisiran	Leqvio		●	●	●		●			●	
	Symptomatic obstructive hypertrophic cardiomyopathy	mavacamten	Camzyos	●		●		●	●	●		●	
Derma-tology	Plaque psoriasis	tapinarof	Vtama						●			●	●
	Pruritus associated with chronic kidney disease	difelikefalin	Korsuva			●			●	●		●	●
Others	Acid sphingomyelinase deficiency	olipudase alfa	Xenpozyme		●	●		●	●	●			
	Detection and visualization of lesions with abnormal vascularity	gadopiclenol	Elucirem			●				●			
	Irritable bowel syndrome with constipation (IBS-C)	tenapanor	Ibsrela	●					●			●	●
	Neovascular age-related macular degeneration (nAMD) or diabetic macular edema	faricimab	Vabysmo		●	●				●			
Totals				12	23	33	6	21	24	30	4	26	19

Source: IQVIA Institute, Jan 2023.

Notes: Includes NASs launched in the U.S. in 2022. Oncology includes supportive care & diagnostics. Information collated from FDA and company releases and relevant clinical trial information. First-in-class based on FDA categorization. Any form of expedited review includes priority review, accelerated approval, breakthrough designation, or fast track determined by the FDA. If the time between the first patent filing (or start of the first clinical trial) and launch in the U.S. is less than or equal to five years this has been noted.

Emerging biopharma companies originated 67% of all new drugs in 2022 and launched 69% of them, reflecting rising independence

Exhibit 31: Companies originating and filing FDA regulatory submissions for NASs and percent of launches by NAS launch year



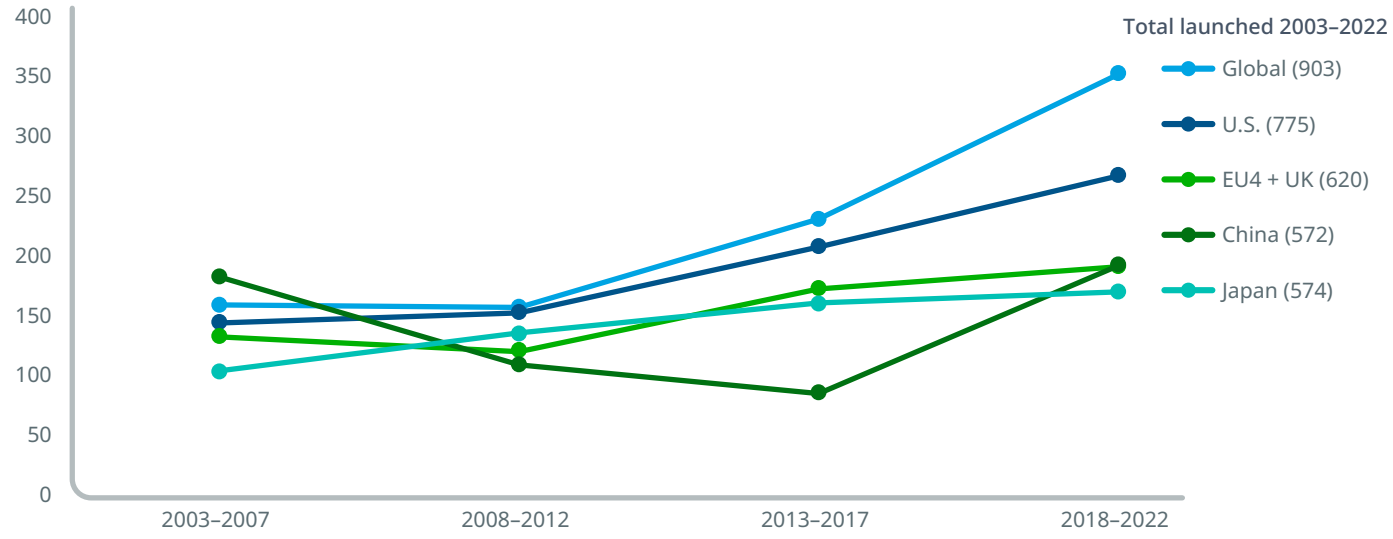
Source: IQVIA Institute, Jan 2023.

- The number of novel active substances (NASs) originated by EBP companies that have launched has doubled in the last five years, with 26 NASs launched in 2022 that originated from an EBP company.
- Although the share of NASs launched that are EBP originated varies significantly from year-to-year, EBP companies have originated 62% of U.S. NAS launches over the past five years, up from 49% over the previous five years and indicating increased EBP innovation reaching the market.
- Products originated by EBPs are increasingly launched by an EBP company, indicating more independence on the part of EBP companies in taking products from innovation to market.
- EBP companies launched 69% of their own products in 2022, with 18 EBP originated and launched NASs. This was the largest share of total NASs that were EBP originated and launched (46%) over the last decade (average = 33%).

Notes: NAS Launches in the U.S. have been segmented by the originator, which is based on the company which filed the first patent. The segmentation laid out in exhibit 1 is applied based on the revenue or R&D spend at the time of the patent filing. Launch company segmentation has been assessed by the FDA filing company, further verified by the status of that company in relation to acquisitions by other companies as often filing company does not change retroactively to reflect new ownership.

A total of 353 novel active substances have launched globally in the past 5 years, bringing the 20-year total to 903

Exhibit 32: Number of novel active substances (NASs) launched globally and in selected countries, 2003–2022



Source: IQVIA Institute, Jan 2023.

- A total of 64 novel active substances have launched for the first time globally in 2022, bringing the five-year total to 353. Based on molecules in the late-stage pipeline, over the next five years an average of 60 NASs are expected to launch annually, expanding the number of NASs launched globally by 300 in the next five years.
- U.S. launches totaled 39 in 2022, the fewest NAS launches in a single year in the U.S. since 2016, likely reflecting delayed impacts of the pandemic, however still totaling a high of 268 in the last five years.
- The four largest EU member countries (France, Germany, Italy, Spain) and the UK saw a similar number of NAS launches to the U.S. in 2022 at 38, below a record number in 2021 of 50 launches; however, the 192 over the past five years lags 76 behind the U.S.
- Japan had 31 NAS launches in 2022, the fifth consecutive year with 30 or more launches, and although launching sooner after global launch than earlier in the century, continuing to lag behind the U.S. and other major markets.
- China's 29 confirmed NAS launches brings the five-year total to 193, with numbers driven by regulatory acceleration mechanisms, such as policies to expedite development and review and reimbursement reforms, all supporting a growing domestic innovation ecosystem and encouraging earlier entry by multi-nationals.

Notes: Novel active substance (NASs) is defined as a medicine with at least one novel ingredient and is noted in the year it launches for the first time in the relevant geography. Fixed-dose combinations are NASs if one of the ingredients is novel but are not if both are previously available. Emergency Use Authorizations (EUAs) are counted as NASs in the year the medicine became available to patients and no exclusion is applied for approval type. COVID-19 vaccines are counted as NASs based on the technology used to create them, with those made by mRNA technology counted as one NAS, and those made by each of eight sub-types of COVID-19 vaccines considered one NAS each, five types have launched to date with three more in development.

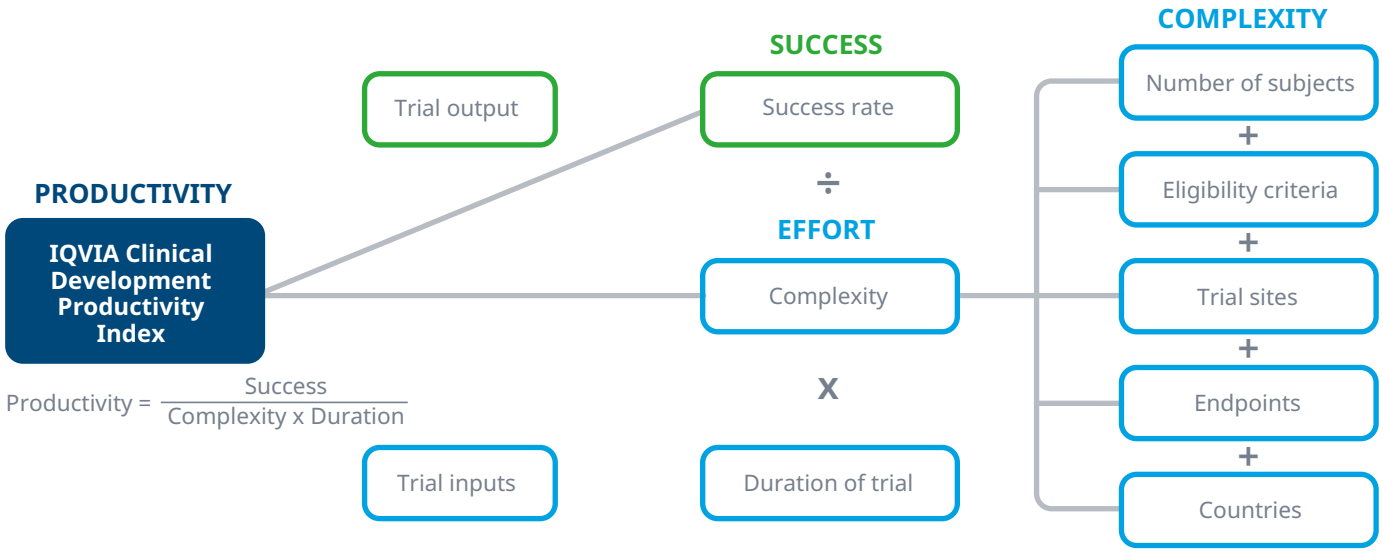
Clinical development productivity

- A Clinical Development Productivity Index provides a composite metric of success rates, clinical trial complexity, and trial duration.
- Clinical development productivity increased dramatically in 2022 driven by a decrease in complexity.
- The composite success rate across all therapy areas fell to 6.3% in 2022 while Phase II and III success rates rose 2–6%.
- Across disease areas, 2022's composite success rate was below the 10-year trend with the exception of vaccines.
- Probability of success varies considerably across diseases, with infectious diseases and dermatology highest.
- Clinical trial complexity declined in 2022, following a significant increase in 2021 due to large COVID-19 trials.
- The declining number of sites for rare diseases and oncology trials is a key driver of the decrease in overall pipeline complexity.
- Trial durations have increased slightly over the past decade and Phase III, in particular, has been a driver in recent years.
- Oncology and rare diseases trial durations have been declining in recent years, attenuating overarching trial duration increases.
- The composite Clinical Development Productivity Index saw an increase in 2022 after steadily declining since 2015.
- Clinical development productivity indices were highest for infectious diseases while oncology extends trend as lowest.

The composite Clinical Development Productivity Index saw an increase in 2022 after steadily declining since 2015.

A Clinical Development Productivity Index provides a composite metric of success rates, clinical trial complexity, and trial duration

Exhibit 33: Clinical Development Productivity Index



Source: IQVIA Institute, Jan 2023.

- The productivity of the clinical development process can be considered as a measure of trial outputs (drugs, innovation, trial success, etc.), compared to a measure of trial inputs or resources dedicated to obtaining those outputs (e.g., aspects of trial complexity, duration, monetary investments, etc.). Such measures of success, complexity, and trial duration were selected for inclusion in the Productivity Index as described above.
- Increases in success will increase productivity overall as will decreases in complexity or duration. Conversely, decreases in success will drive down the Productivity Index, as do increases in complexity and duration.
- To obtain current-state measures of trial complexity (mean number of endpoints, sites, countries, patients, eligibility criteria) as well as data on trial duration, attributes were leveraged from the Citeline Trialtrove clinical trial database. In order to determine the number of eligibility criteria and endpoints from the unstructured or semi-structured text in trial records, natural language processing was used to identify common formatting patterns employed by trial sponsors in detailing these features. Success metrics were calculated from IQVIA™ Pipeline Intelligence based on medicines progressing to a subsequent research phase or being discontinued, suspended, withdrawn, or becoming inactive for three or more years (see Methodology). Each metric in each phase for each disease is indexed to the equivalent 2010 value for all diseases. Indices are available for each phase or as an average across phases.
- An analysis of productivity was conducted across all trials started between 2010 and 2022, with details included for therapy areas: cardiovascular, dermatology, infectious diseases, endocrinology, immunology, neurology, oncology, respiratory, vaccines (separately from infectious diseases), and rare diseases.

Clinical development productivity increased dramatically in 2022 driven by a decrease in complexity

Exhibit 34: Clinical Development Productivity Index and elements of productivity indexed to 2010 values

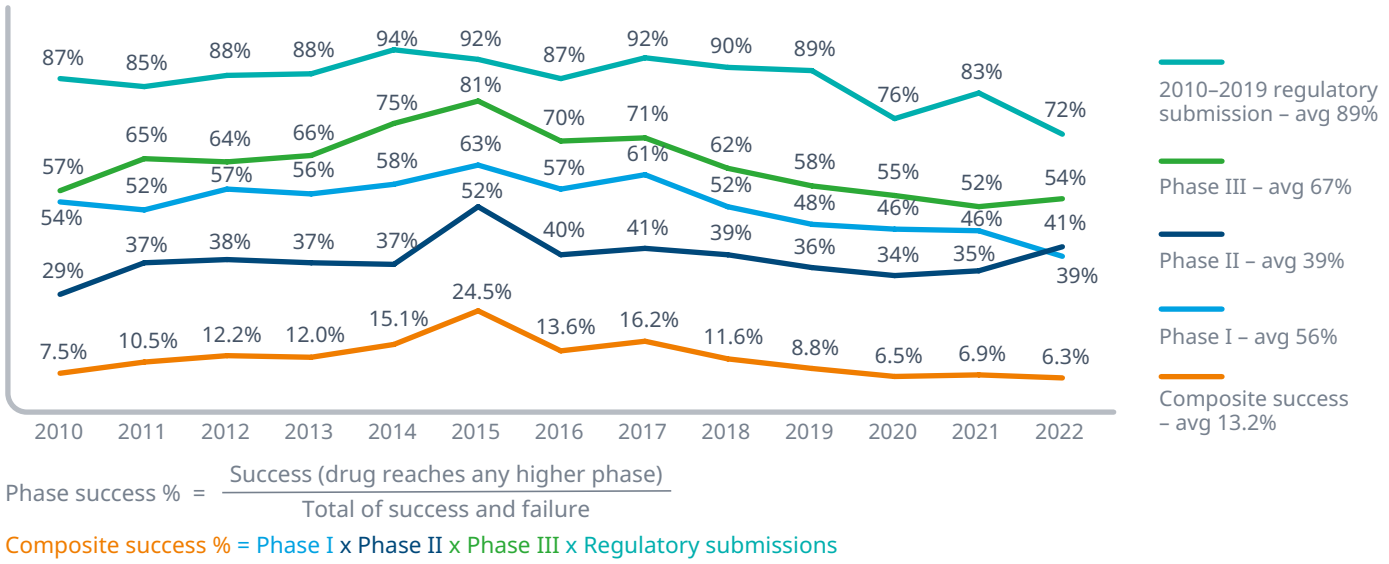
Source: IQVIA Pipeline Intelligence, Dec 2022; Citeline Trialtrove, IQVIA Institute, Jan 2023.

- Clinical development productivity — a composite metric of success rates, clinical trial complexity, and trial duration — rebounded in 2022, reversing a 10-year downward trend. Trial complexity returned to the previous trend after an outlier high in 2021, while overall success rates improved slightly.
- Trial success rates were consistent with the baseline, indexing up slightly from 2021 but well below the highs of the past 10 years.
- Trial complexity dropped sharply in 2022 after unusually high levels in 2021, which were driven by larger numbers of study subjects. All other components of the complexity indices declined slightly in 2022.
- Trial durations have remained essentially flat from 2017, reflecting difficulties in recruiting patients for more rare diseases and longer follow-up periods after treatment, even as some trials have been exceptionally faster than historic norms.

Notes: Success rates and durations are indexed to the mean value for all diseases in 2010 equal to 1. The five complexity metrics are indexed to all diseases in 2010 equal to 1, and then summed, equaling 5.

The composite success rate across all therapy areas fell to 6.3% in 2022 while Phase II and III success rates rose 2–6%

Exhibit 35: R&D composite success rate and average phase success rates Phase I to filing, 2010–2022



$$\text{Phase success \%} = \frac{\text{Success (drug reaches any higher phase)}}{\text{Total of success and failure}}$$

Composite success % = Phase I x Phase II x Phase III x Regulatory submissions

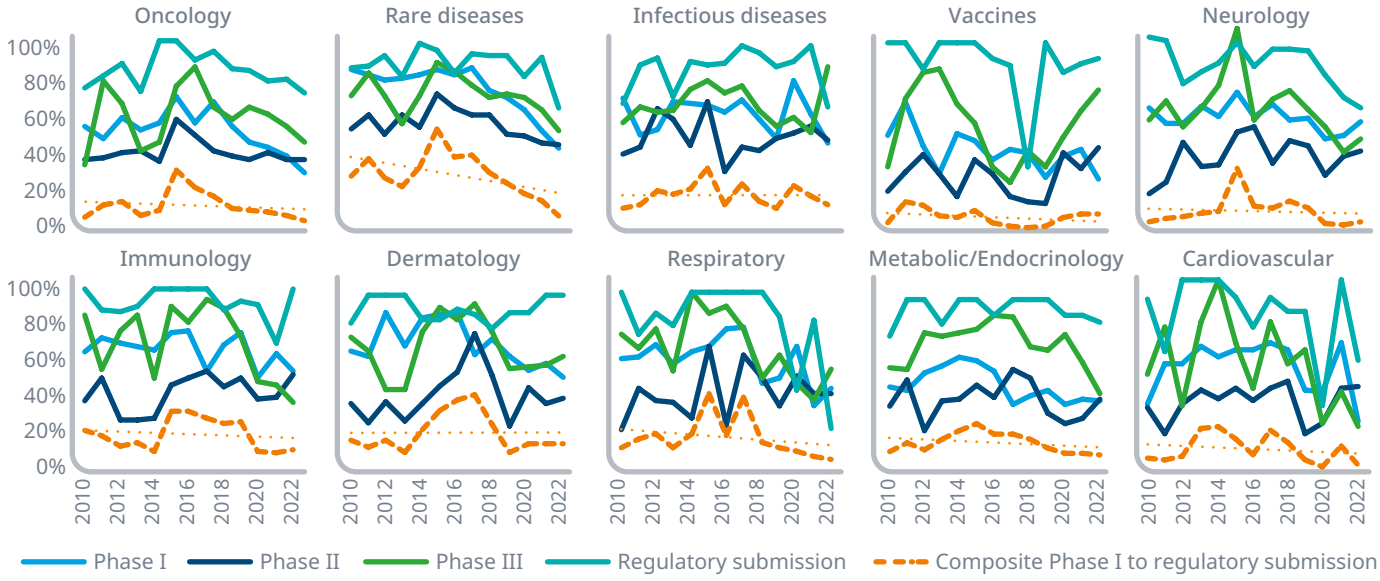
Source: IQVIA Pipeline Intelligence, Dec 2022; IQVIA Institute, Jan 2023.

- The composite success rate for the pipeline fell to a 10-year low in 2022, but embedded an increase in Phase II and III rates, offsetting declines in Phase I and at regulatory submission.
- Phase II success rates increased from 35% to 41% in one year, returning to the level last seen in 2017.
- Phase III rates rose to 54%, still far below the 67% 10-year pre-pandemic average.
- The pandemic has continued to disrupt the trials which are completed, and some trials which were understood to have failed in recent years due to extended inactivity had actually been continuing and have now completed successfully, resulting in retroactive restatement of past years success rates. The overall composite success rate in last year's report was 5.2%, compared to the restated 6.9% in the current analysis.
- Phase I success rates dropped to 39%, a low since 2010 and down 7% from the 2021 rate.
- Success rates for products filing for regulatory approval also reached a low level, dropping to 72% in 2022.

Notes: Phase success rates are calculated as the percentage of products reaching a subsequent phase in the year out of the total of products with an outcome including those which are discontinued, suspended or withdrawn as well as those which have been inactive for three years. The date three years after the last update determines which year the drug is considered to have gone inactive and become included in the denominator of the success rate, except when desk research has concluded the drug is still in active research. Product's research status is assessed in any geography globally.

Across disease areas, the 2022 composite success rate was below the 10-year trend except for vaccines

Exhibit 36: R&D phase and composite success rates by therapy area, 2010–2022



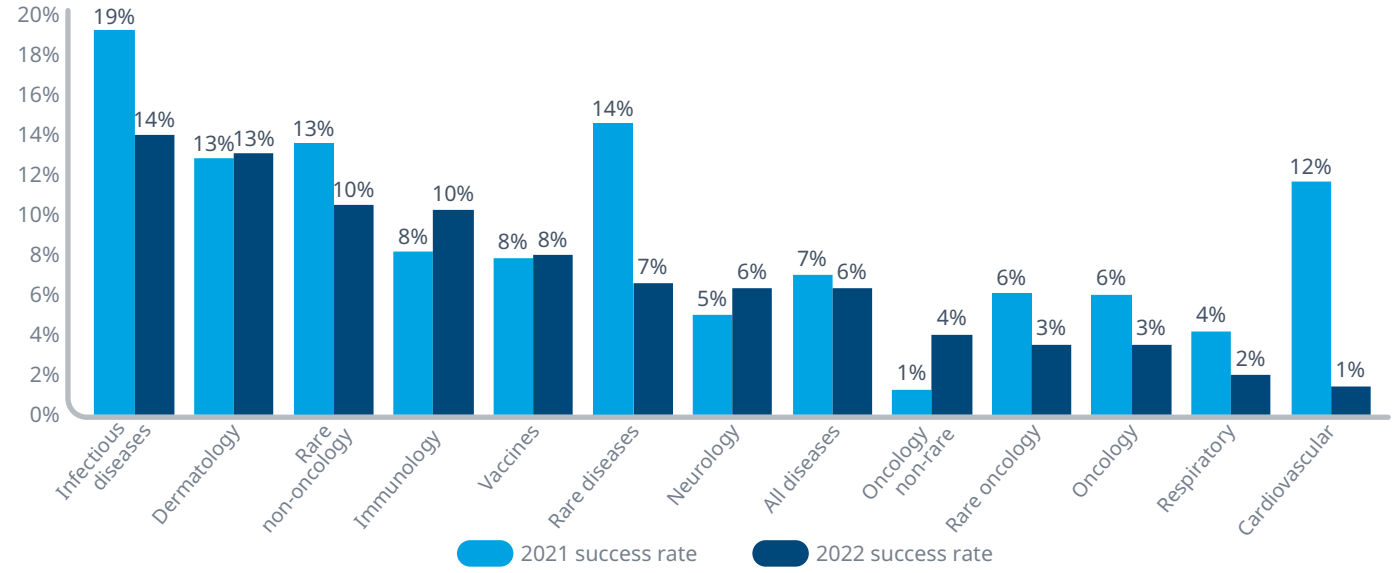
Source: IQVIA Pipeline Intelligence, Dec 2022; IQVIA Institute, Jan 2023.

- 2022's composite success rate of 6.3% was lower than the 10-year trendline in neurology, oncology, respiratory and cardiovascular classes.
- While most disease areas worsened in 2022, almost all had prior years restated as research previously thought to have become inactive had new progress or updated activity.
- While activity levels remained resilient during the pandemic, oncology and rare diseases — the two largest segments of the R&D pipeline — all saw substantial decreases in composite success rates in 2022, continuing a trend over recent years.
- Vaccines, which had seen declining success from 2016 to 2019, saw significant increases in success except in Phase I in 2022, mostly driven by the success of COVID-19 vaccines.
- Infectious diseases composite success declined slightly in 2022, continuing below the trendline for the observed period, driven by falling Phase I and regulatory submission successes.

Notes: Phase success rates are calculated as the percentage of products reaching a subsequent phase in the year out of the total of products with an outcome including those which are discontinued, suspended or withdrawn as well as those which have been inactive for three years. The date three years after the last update determines which year the drug is considered to have gone inactive and become included in the denominator of the success rate, except when desk research has concluded the drug is still in active research.

Probability of success varies considerably across diseases, with infectious diseases and dermatology highest

Exhibit 37: R&D composite success rate by therapy area in 2021 and 2022



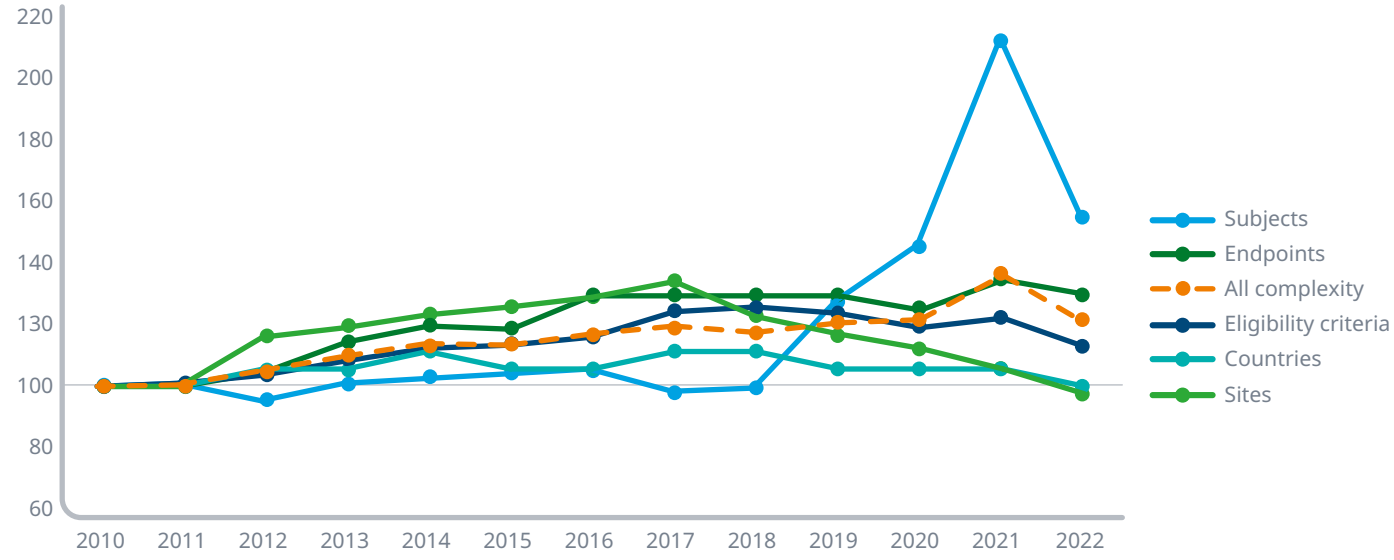
Source: IQVIA Pipeline Intelligence, Dec 2022; IQVIA Institute, Jan 2023.

- The drop in composite success rate in 2022 overlays a complex set of dynamics across therapeutic segments, which in 2021 ranged from 1% to 19%, and in 2022 showed a narrower range from 1% to 14%.
- Infectious diseases, dermatology, and non-oncology rare diseases had the highest composite success rates in 2022, the same or slightly lower than their 2021 level.
- Oncology, the largest segment of the pipeline, is currently seeing composite success rates of 3%, with slight differences between rare cancers (3%) and non-rare cancers (4%).
- Rare diseases had a composite success rate of 7% in 2022, down from 14% in the prior year, reflecting highly dynamic results in these types of drugs.
- Products for cardiovascular disease saw success in 2021 of 12%, more consistent with long-term trends with 2020 and 2022 both representing unusually low success rates. It remains to be seen whether these outlier periods will continue.

Notes: Phase success rates are calculated as the percentage of products reaching a subsequent phase in the year out of the total of products with an outcome including those which are discontinued, suspended or withdrawn as well as those which have been inactive for three years. The date three years after the last update determines which year the drug is considered to have gone inactive and become included in the denominator of the success rate, except when desk research has concluded the drug is still in active research.

Clinical trial complexity declined in 2022, following a significant increase in 2021 due to large COVID-19 trials

Exhibit 38: Elements of complexity indexed to 2010 values, all phases 2010–2022



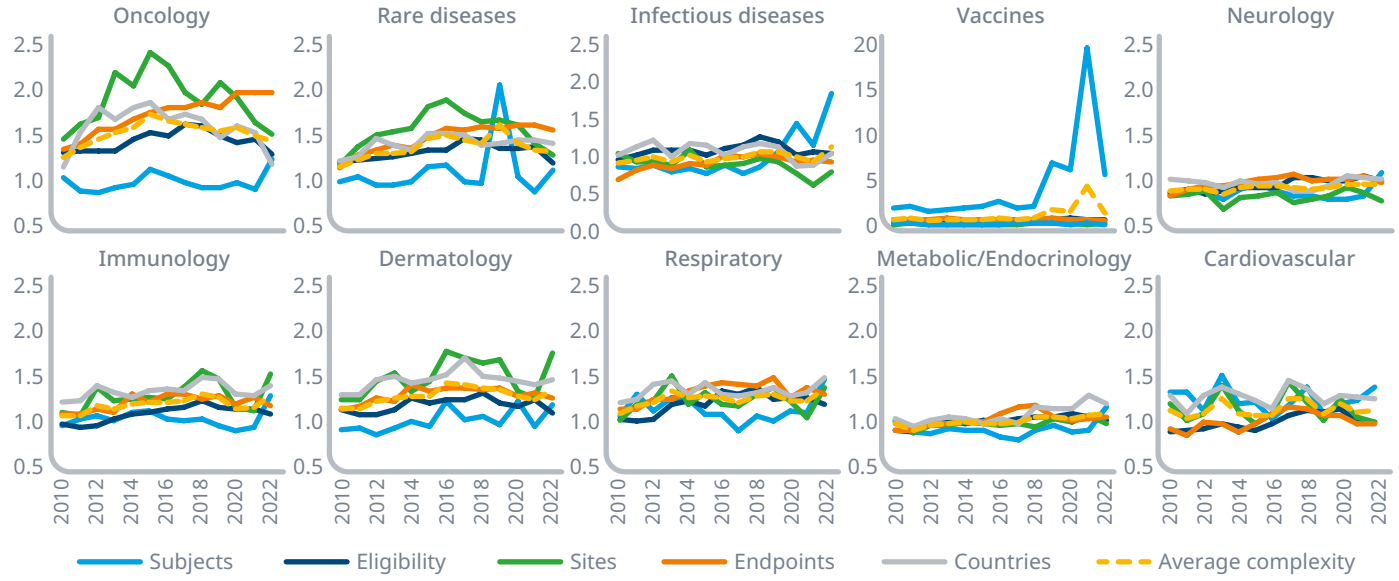
Source: Citeline Trialtrove, IQVIA Institute, Jan 2023.

- Following a period of increasing complexity in the first half of the last decade, trial complexity jumped in 2021 to an index of 136 compared to 2010 before dropping back to 121 in 2022, while still exceeding prior years.
- The unusually high number of trial subjects in 2021, mainly in COVID-19 trials, is the main driver of lower overall complexity in 2022.
- The drop in the number of sites and the number of countries across industry trials was another driver of the decline in 2022, with sites 2.5% below 2010 levels and countries returning to the baseline index of 100, and some of the reduction in these metrics driven by ongoing COVID-19 trial disruptions and the conflict in Ukraine.
- The number of subjects on average has increased dramatically since 2018, with the 2021 index of 212 and 2022 at 154, both as a result of large-scale COVID-19 vaccine trials.
- As the COVID-19 pandemic subsides, the number of clinical trial subjects is likely to return to pre-pandemic levels.
- These measures, while not definitive in determining the complexity of operating a trial, do provide a useful guide for the ongoing effort associated with trials.

Notes: Terminated and withdrawn trials were excluded from the analysis. Trials were industry sponsored and interventional. Diagnostics, behavioral therapies, supplements, devices, and medical procedures were excluded. Infectious diseases excludes vaccines.

The declining number of sites for rare diseases and oncology trials is a key driver of the decrease in overall pipeline complexity

Exhibit 39: Trial complexity by element and therapy area, 2010–2022



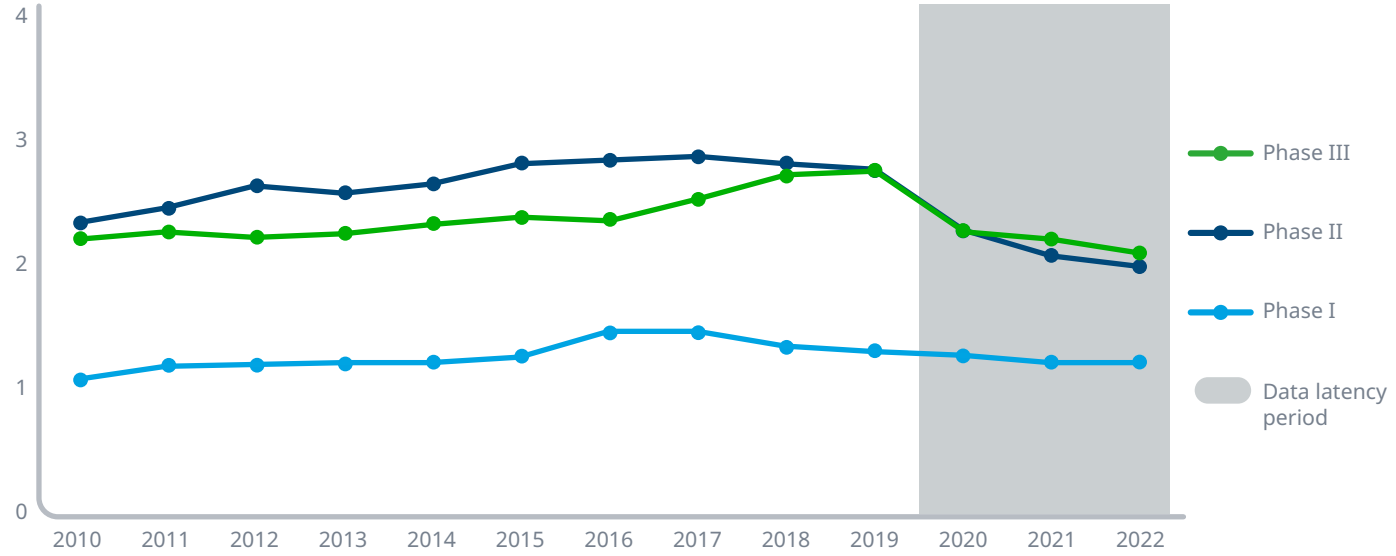
Source: Citeline Trialtrove, IQVIA Institute, Jan 2023.

- In line with decreases in overall complexity, most of the evaluated therapy areas showed a decline in 2022.
- Oncology trials, which are among the most complex using the index, saw a drop in complexity in 2022 to its lowest level since 2011. As with the pipeline in general, this drop is highly correlated with the drop in number of sites and countries, which began in 2015 but was amplified by the pandemic. The number of subjects did increase sharply in 2022, however, perhaps related to a shift away from rare cancers.
- Rare disease trials have been showing a steady decline in complexity since 2015 due to a declining number of sites and subjects, indicating more focus on smaller patient populations with the exception of large Ebola trials started in 2019. Fewer sites for rare disease trials was a notable inflection in the last three years.
- In recent years, vaccine trials have become increasingly larger than other trials and vary considerably in the number of subjects by disease target, with much larger trials in Ebola, influenza, and COVID-19 driving the increase in recent years.

Notes: Terminated and withdrawn trials were excluded from the analysis. Trials were industry sponsored and interventional. Diagnostics, behavioral therapies, supplements, devices, and medical procedures were excluded. Infectious diseases excludes vaccines.

Trial durations have increased slightly over the past decade, and Phase III, in particular, has been a driver in recent years

Exhibit 40: Average trial duration in years by phase, all therapy areas, 2010–2022



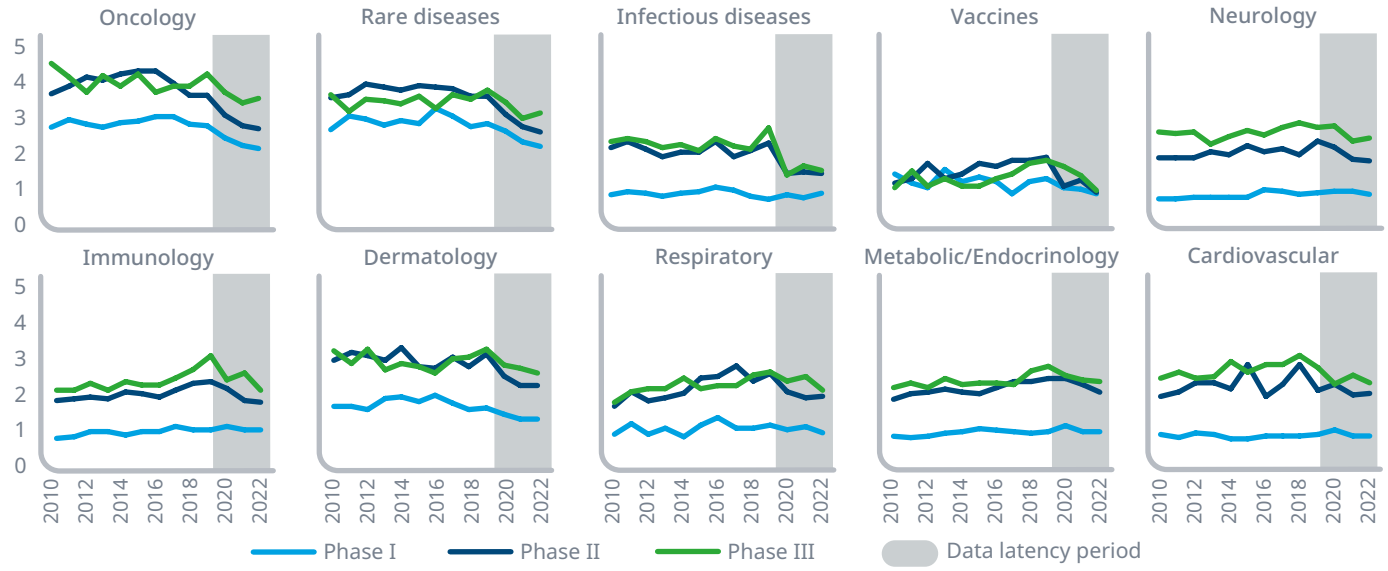
Source: Citeline Trialtrove, IQVIA Institute, Jan 2023.

- Trials started in recent years may have durations based on planned completion versus actual confirmed dates, which could be artificially driving this trend down, especially during disruptions caused by the COVID-19 pandemic, making the latest three years an unreliable guide to the expected trends.
- Prior to 2019, Phase III trials saw a moderate increase in trial duration — up to, on average, 2.7 years in 2018 compared to 2.2 years in 2010.
- Prior to the most recent three years, the majority of trial durations were based on actual completion, whereas the most recent periods have less than 50% of trials with actual dates and include a mix of very accelerated actual trials as well as potentially unrepresentative estimates from sponsors.
- As a result of these data latency issues, the duration information for 2019 is used for 2020 to 2022 in productivity indices elsewhere in this report, and these indices may be restated in later updates as actual durations are more reliably reported.

Notes: Trial durations are calculated as the time between trail start and the completion of the primary endpoints even as some trial activity may continue after this. In the data latency period, more than 50% of trials report planned end dates, which in combination with actual end dates that are unusually rapid, skew the durations downward in a pattern which is consistently restated over time. For analysis in the development productivity index, the last pre-latency period (2019) is used as the duration for the subsequent years.

Oncology and rare disease trial durations have been declining in recent years, attenuating overarching trial duration increases

Exhibit 41: Average trial duration (years) by phase and therapy area, 2010–2022



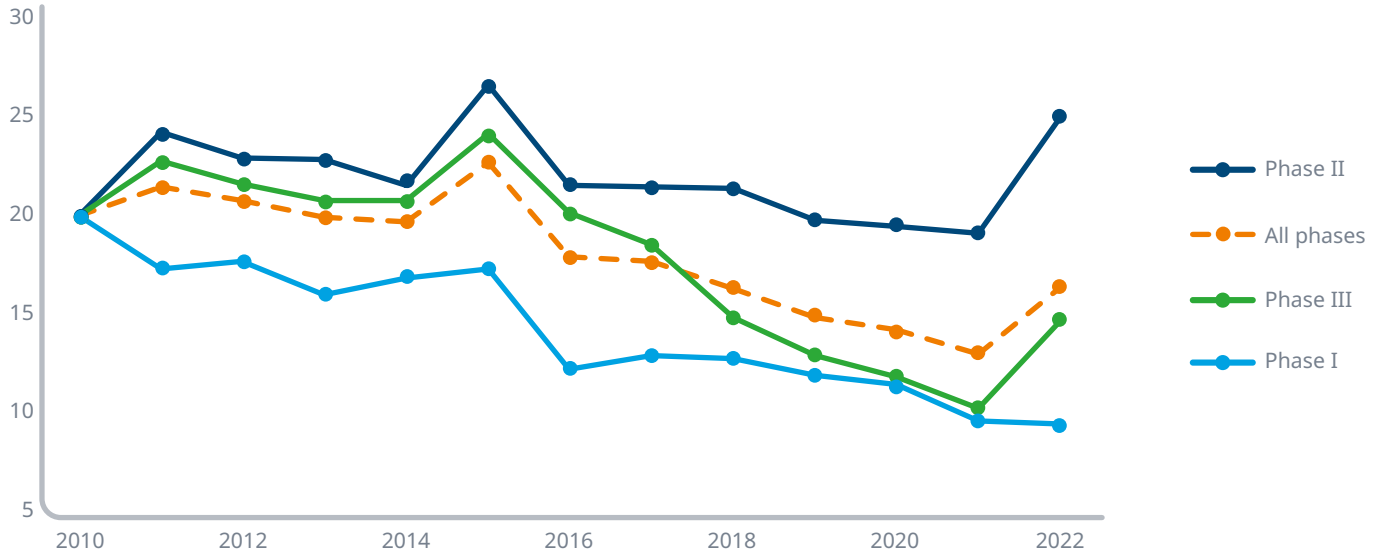
Source: Citeline Trialtrove, IQVIA Institute, Jan 2023.

- Trial durations for different disease areas have been generally stable over the last decade, excluding the data latency period in the last three years.
- Phase I trials are often very short, with all but oncology, rare diseases, vaccines, and dermatology averaging less than a year.
- Total (all phases) oncology duration has come down by an average of 1% per year through 2018, with Phase II trials decreasing in duration at the greatest rate.
- Oncology and rare diseases have the longest timelines in general across the disease areas, likely due to difficulties in finding and recruiting patients as well as extended observation periods to demonstrate treatment efficacy.

Notes: Terminated and withdrawn trials were excluded from the analysis. Trials were industry sponsored and interventional. Diagnostics, behavioral therapies, supplements, devices, and medical procedures were excluded. Trial duration is based on trial dates reported in clinical trial databases. Trial start date is the date on which the enrollment of participants for a clinical study began. Trial end date corresponds to when the trial ended or is expected to end. Vaccine trials are infectious disease only. Phase II includes Phases I/II, II, IIa, IIb. Phase III includes Phase II/III and III. Infectious diseases excludes vaccines.

The composite Clinical Development Productivity Index saw an increase in 2022 after steadily declining since 2015

Exhibit 42: Clinical development productivity by phase and overall, 2010–2022



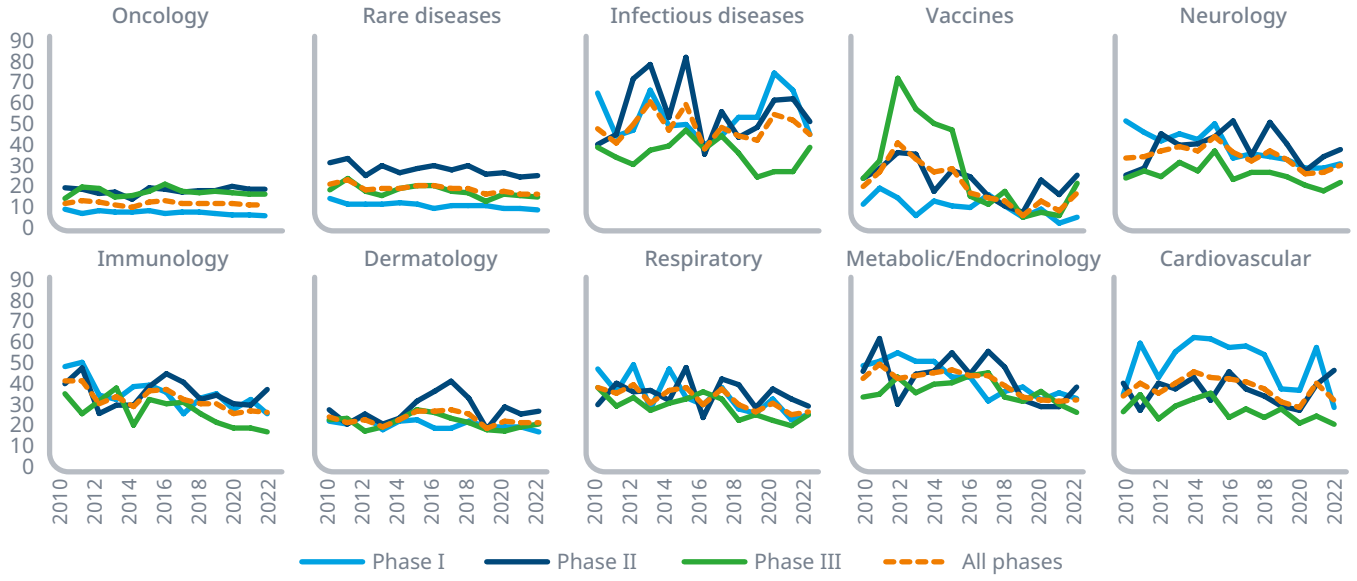
Source: IQVIA Pipeline Intelligence, Dec 2022; Citeline Trialtrove, IQVIA Institute, Jan 2023.

- The composite Clinical Development Productivity Index has dropped by 22% over the past decade.
- All phases of clinical development showed declines in productivity in 2021, however Phase II and III rebounded in 2022, lifting overall productivity from 12.9 to 16.3, where the 2010 index is 20.
- Phase II trials have consistently been above the overall index as success rates have remained more stable and trial durations have declined slightly, but success rates increased dramatically in Phase II in 2022, lifting overall productivity.
- Phase III trials had seen a significant decline in productivity over the past five years, primarily due to decreasing probability of success and increasing durations, but rebounded as complexity dropped in the latest year.
- While there is a great variability among therapy areas, the overall downward trend in productivity is believed to be a result of slowly increasing clinical trial timelines and decreasing probability of success, even as clinical trial complexity has seen modest reductions in recent years.

Notes: Terminated and withdrawn trials were excluded from the analysis. Trials were industry sponsored and interventional. Diagnostics, behavioral therapies, supplements, devices, and medical procedures were excluded. Trial duration is based on trial dates reported in clinical trial databases. Trial start date is the date on which the enrollment of participants for a clinical study began. Trial end date corresponds to when the trial ended or is expected to end. Phase II includes Phases I/II, II, IIa, IIb. Phase III includes Phase II/III and III. Infectious diseases excludes vaccines.

Clinical development productivity indices were highest for infectious diseases while oncology extends trend as lowest

Exhibit 43: Clinical development productivity across all phases by therapy area, 2010–2022



Source: IQVIA Pipeline Intelligence, Dec 2022; Citeline Trialtrove, IQVIA Institute, Jan 2023.

- The Clinical Development Productivity Index varies widely across therapeutic areas, with a low of 8.6 for oncology and a high of 36.5 for infectious diseases.
- Oncology and rare diseases have consistently had among the lowest productivity rates across the last 10 years. These areas show significant overlap and are kept to a modest productivity based on similar declines in success and high complexity.
- Vaccine productivity increased substantially in 2022, driven by higher success rates in Phase II and III.
- Cardiovascular products had a drop in productivity in 2022, resuming the downward trend over the past decade and including a continued low phase III productivity.

Notes: Terminated and withdrawn trials were excluded from the analysis. Trials were industry sponsored and interventional. Diagnostics, behavioral therapies, supplements, devices, and medical procedures were excluded. Trial duration is based on trial dates reported in clinical trial databases. Trial start date is the date on which the enrollment of participants for a clinical study began. Trial end date corresponds to when the trial ended or is expected to end. Vaccine trials are infectious disease only. Phase II includes Phases I/II, II, IIa, IIb. Phase III includes Phase II/III and III. Infectious diseases excludes vaccines.

Productivity enablers

- Innovations are progressing through maturation cycles to enable clinical productivity improvements even as they contribute to evolving industry disruptions and delivery complexities.
- Scientific complexity continues to increase, with first-in-class therapies in 62% of launches spread across nearly all major therapeutic areas in 2022.
- Regulatory agencies are re-evaluating their procedures, protocols and requirements to address system-wide changes resulting in a rapidly evolving landscape for innovators.
- Trials run with novel trial designs have increased from 7.5% of trial starts in 2010 to 17.0% in 2022, more than half in oncology.
- Novel trial designs are more complex and lengthier compared to traditional trials but are associated with faster total program times.
- Trials which are remote, virtual or decentralized (RVD) have been increasing in line with the industry trial starts, with a slight dip in 2022.
- RVD trials involve more subjects, sites, countries, and endpoints but have shorter durations than traditional trials.
- The use of real-world evidence as part of FDA approval decisions dropped in 2022 even as FDA increases its focus on enabling use of RWE in clinical submissions.
- Most new drugs received expedited reviews, with increases in priority and breakthrough designations in 2022.
- Recent approvals often receive some form of expedited review which, on average, includes relatively fewer patients and therefore lower trial complexity.
- Twenty-three drugs were launched less than five years into their patent terms in the past three years, up from 15 in total from 2012–2019.
- Some therapy areas have significantly shorter trial durations and 'white space' before starting a subsequent research phase.
- Enablers such as AI/ML are showing increasing potential impact on clinical development productivity as innovative research candidates advance into the clinical development pipeline.

As technology and data advances take hold across the pharmaceutical development pipeline, productivity is being impacted by a range of trade-off effects on complexity, timing, and probability of success.

Innovations are enabling scientific productivity improvements, but implementation realities also bring challenges

Exhibit 44: Framework of innovative productivity enablers impact on clinical development productivity

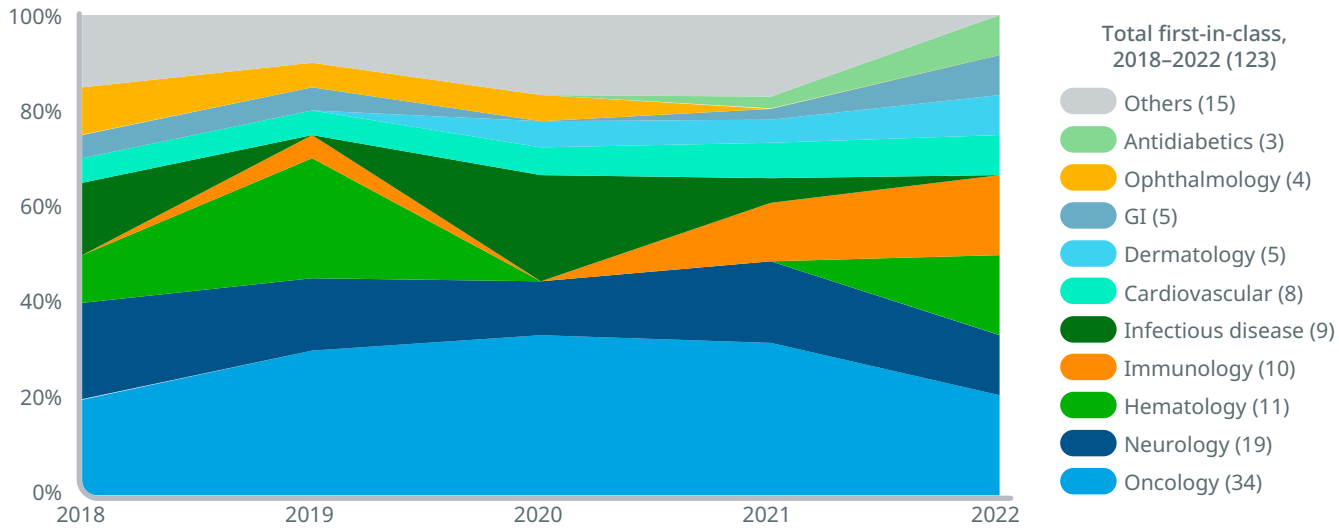
		INNOVATIONS/PRODUCTIVITY ENABLERS					
+ Productivity Enabler / + Potential Productivity Enabler / – Current Productivity Challenge		HIGHER MATURITY ← ENABLER MATURITY → LOWER MATURITY					
PRODUCTIVITY DISRUPTORS		BIOMARKERS	NOVEL TRIAL DESIGNS	DECENTRALIZED METHODS /DEVICES AND DIGITAL ENDPOINTS	RWD COLLECTION /RWE SUBMISSION	AI/ML	IN SILICO /TRIAL SIMULATION
Accelerated scientific innovation	Novel therapeutic platforms					+	+
	New targets / Novel MOAs	+	+	+	+	+	+
	New endpoints	+	+	+	+	+	+
Evolving stakeholder roles / needs	Patient privacy			–	–	–	–
	Patient representativeness	+ / –	+ / –	+ / –	+	+	+
	Shifting site footprint	+ / –	+ / –	+ / –	+	+	+
	Global regulatory changes	+ / –	+ / –	+ / –	+ / –	–	–

Source: IQVIA Research and Development Solutions expertise, IQVIA Institute, Jan 2023.

- As technology and data advances take hold across the pharmaceutical development pipeline, productivity is impacted by a range of trade-off effects on complexity, timing and probability of success.
- Increasing incorporation of scientific breakthroughs, fueled by ongoing genomics and multi-dimensional patient data advances and maturation of multiple novel therapeutics platforms, has increased risk and complexity as novel mechanisms of action are validated in the clinical pipeline.
- Addressing evolving stakeholder roles and needs in clinical development — especially evolving global regulatory responses to recent clinical innovation — has also introduced uncertainty and need for process redesign, but promises to improve clinical development productivity as new equilibriums are reached.
- Innovative enablers are now starting to deliver against productivity disruptions and opportunities. Incorporation of biomarkers, novel trial designs, and decentralized/direct to patient methodologies are yielding initial productivity gains with promise to bring more as technology implementation and cross-stakeholder processes are optimized.
- Longer range innovations including use of RWE in clinical submissions and decisions, leverage of AI/ML across the entire R&D cycle, and use of trial simulations are poised to bring about significant productivity gains as they operationally mature in the clinical pipeline.
- Challenges in scaling new technology (including enabling sites and leveraging step-change increases in available data to create information) is foundational to transitioning current productivity challenges into productivity gains.

Innovative first-in-class NAS launches spread across nearly all significant therapy areas in 2022

Exhibit 45: Therapy area share of first-in-class U.S. novel active substances (NASs), 2018–2022



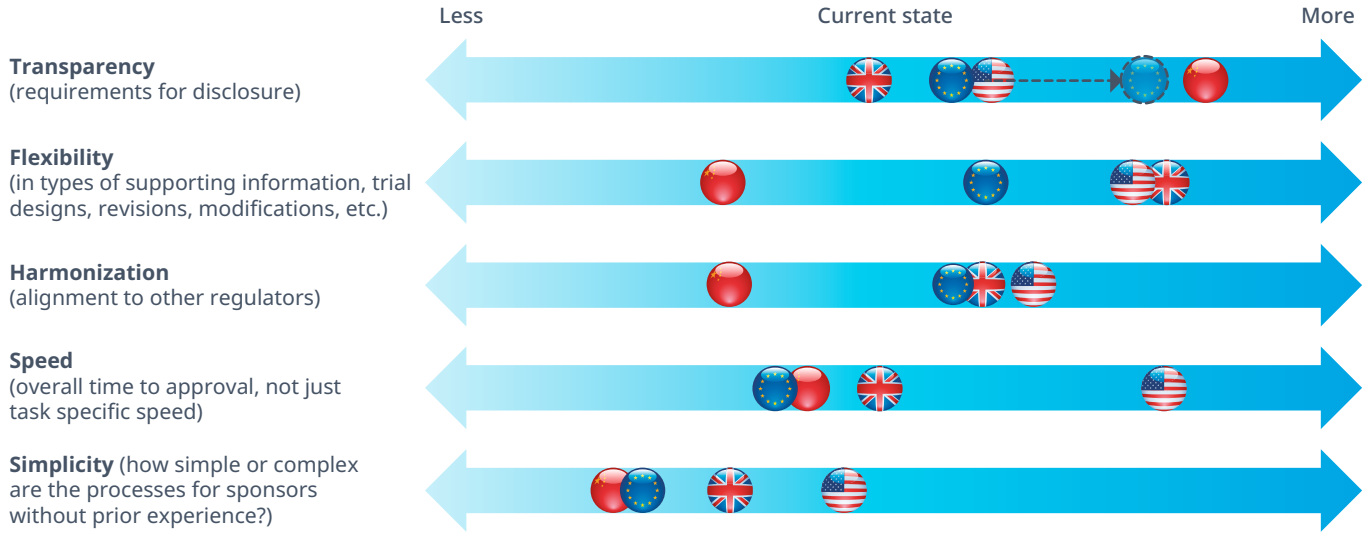
Source: IQVIA Institute, Jan 2023.

- First-in-class molecules accounted for 62% of NAS launches in 2022 (Exhibit 29), up from 41% in 2019.
- As a function of expanded first-in-class representation across launched molecules, recent years have seen first-in-class launches across each of the top therapeutic areas.
- In 2022, first-in-class molecules represented 100% of antidiabetic, dermatology, gastrointestinal, and cardiology, and 5% and 50% of oncology and neurology launches, respectively.
- The antidiabetic focus on first-in-class launches comes after no novel mechanism launches in the past two years.
- There have been no first-in-class infectious disease launches since the COVID-19 driven peak in 2020.
- Notably, 79% of the first-in-class molecules launched in 2022 received some form of expedited development or review (e.g., Priority Designation, Accelerated Approval, Breakthrough Designation, or Fast Track) versus 73% of follow-on molecules. This is a slightly lower alignment of molecule novelty to expedited designation versus the average since 2012, where some form of expedited review has been seen for 77% of the first-in-class launches, versus 59% for follow-on mechanisms.

Notes: A novel active substance (NAS) is a new molecular or biologic entity or combination where at least one element is new; Includes NASs launched in the United States 2018-2022 regardless of the timing of FDA approval. First-in-class is based on FDA classification.

Regulatory agencies are shifting their procedures, protocols, and requirements resulting in an evolving landscape for innovators

Exhibit 46: Comparative analysis of key characteristics of global pharmaceutical regulatory agencies

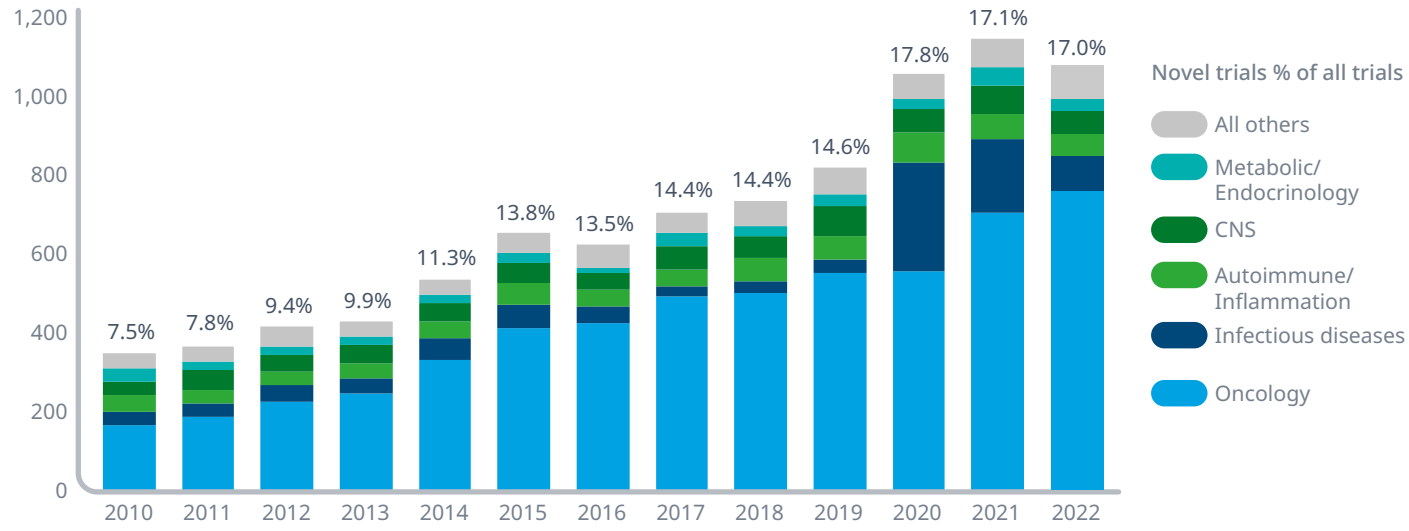


Source: IQVIA Global Regulatory Network expert input; IQVIA Institute, Jan 2023.

- Global regulatory agencies are contending with the range of scientific, technical, and policy changes in the human health space, leading to a spectrum of responses that are impacting drug developers as they execute global clinical programs.
- Focus on transparency continues across geographies, especially with EU ongoing Clinical Trial Regulation (CTR) implementation, but all are challenged to varying degrees by privacy and competitive complexities.
- The U.S., UK, and China are focused on fast track programs and enabling novel trial designs to allow flexible acceleration.
- The EU is working through additional challenges to align flexible options across member states.
- The U.S. and China have a visible focus on harmonization, especially around decentralized trials and novel trial approaches, while the EU CTR lays out ambitious harmonization targets with the potential for implementation challenges.
- Ongoing U.S. implementation of fast track and accelerated approval mechanisms continues to yield acceleration, and recent Chinese focus and staff investment have reduced approval timelines.
- The EU and UK are currently lagging on accelerated pathway impact due to implementation challenges.
- Ongoing cross geography regulatory efforts to simplify submission processes struggle to keep pace with innovation driven shifts and complexities across all facets of the pharmaceutical clinical development process.

Novel trial designs have increased from 7.5% of trial starts in 2010 to 17.0% in 2022, more than half in oncology

Exhibit 47: Novel trial design starts by year and therapy area, 2010–2022



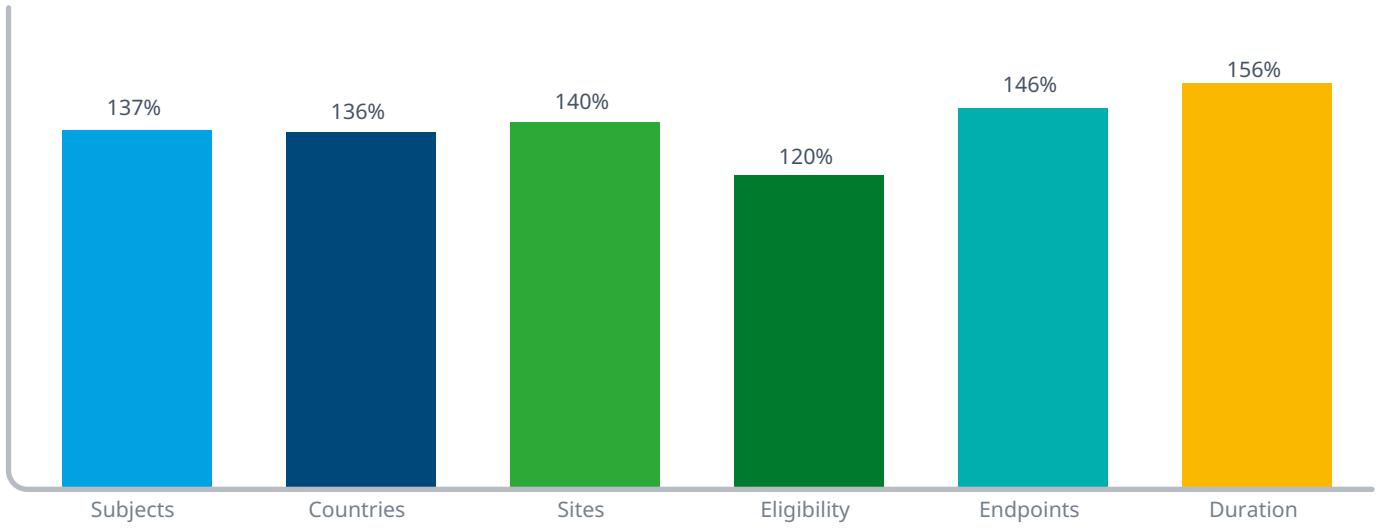
Source: Citeline Trialtrove, IQVIA Institute, Jan 2023.

- Novel trial designs, including umbrella, basket, master, and adaptive protocols, are steadily increasing in their proportion of the industry trial pipeline, with 1,068 trials (17% of new and planned trial starts), including one or more aspects of novel trial design in 2022.
- Oncology trials drive the highest amount of novel design activity in the pipeline, and 2022 showed the highest number of these cancer trials to-date. Novel trial designs were found in 27.3% of the 2,334 oncology trials started in 2022 — 10 percentage points higher than 17% for the pipeline overall.
- The last three years have seen a significant increase in novel design use in infectious diseases, with COVID-19 trials widely leveraging master protocols and adaptive structures to enable parallel processing, accelerated program data collection, and better decision-making.

Notes: Trials were industry sponsored, interventional trials and device trials were excluded. Novel trial designs include umbrella, basket, adaptive, master protocol, dose escalation + dose expansion studies using a range of keyword strings.

Novel trial designs are more complex and lengthier compared to traditional trials but are associated with faster total program times

Exhibit 48: Trials with novel trial designs compared to those with traditional trial designs, 2010–2022



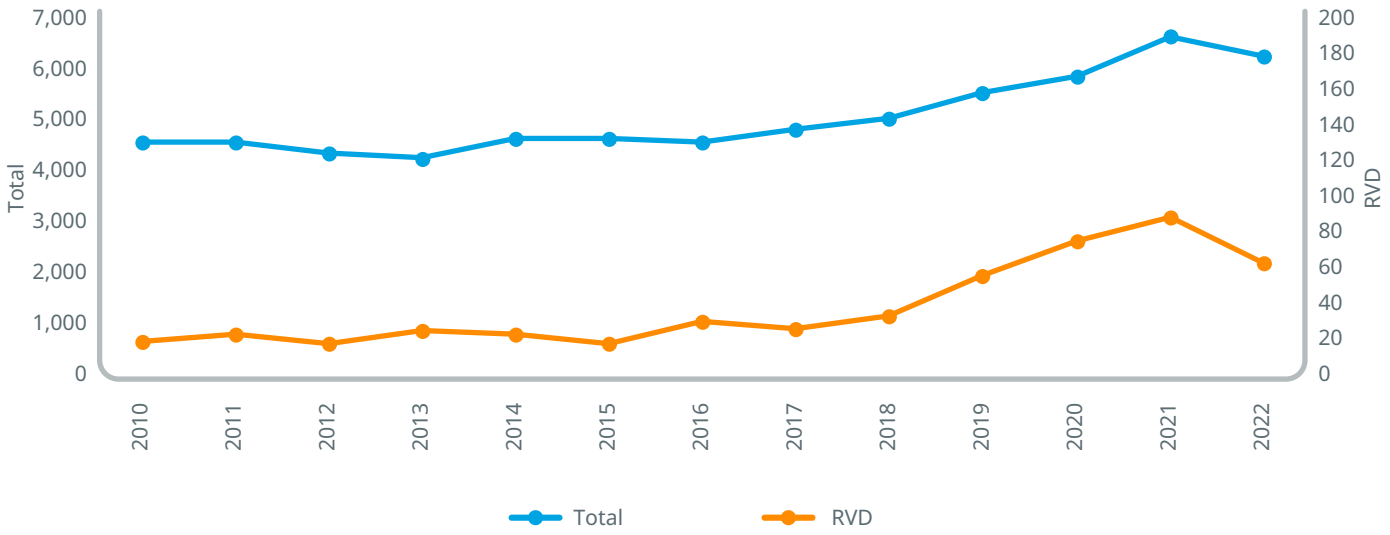
Source: Citeline Trialtrove, IQVIA Institute, Jan 2023.

- Analysis of individual trials that used novel trial designs (including combined phase trials and master/umbrella protocols) showed elevated complexity and timing versus key trial metrics for non-novel trial designs.
- For trials with novel designs, the numbers of subjects, trial sites, primary and secondary endpoints, and the duration of trials are all between 20 and 45 percent higher than those with traditional designs.
- The overall 36% increase in complexity and 56% increase in trial duration is consistent with the use of adaptive trials, which are designed to enrich the information gathered in combined-phase protocols to best inform the next trial(s).
- When analyzed on a per trial basis, combined-phase trials are more complicated and lengthier but contribute to shorter program times with earlier information collection and a reduction in total number of trials, phase transitions, and white space to bring a drug to the market.

Notes: Includes industry sponsored, interventional trials excluding devices. Novel trial designs include umbrella, basket, adaptive, master protocol, dose escalation + dose expansion studies using a range of keyword strings. Trial attributes from Citeline Trialtrove for the identified trials were compared to the 12-year cohort of all other trials that were not included in the novel design cohort.

Trials which are remote, virtual or decentralized have been increasing in line with industry trial starts, with a slight dip in 2022

Exhibit 49: Trial starts for all trials and remote, virtual or decentralized trials (RVD), 2010–2022



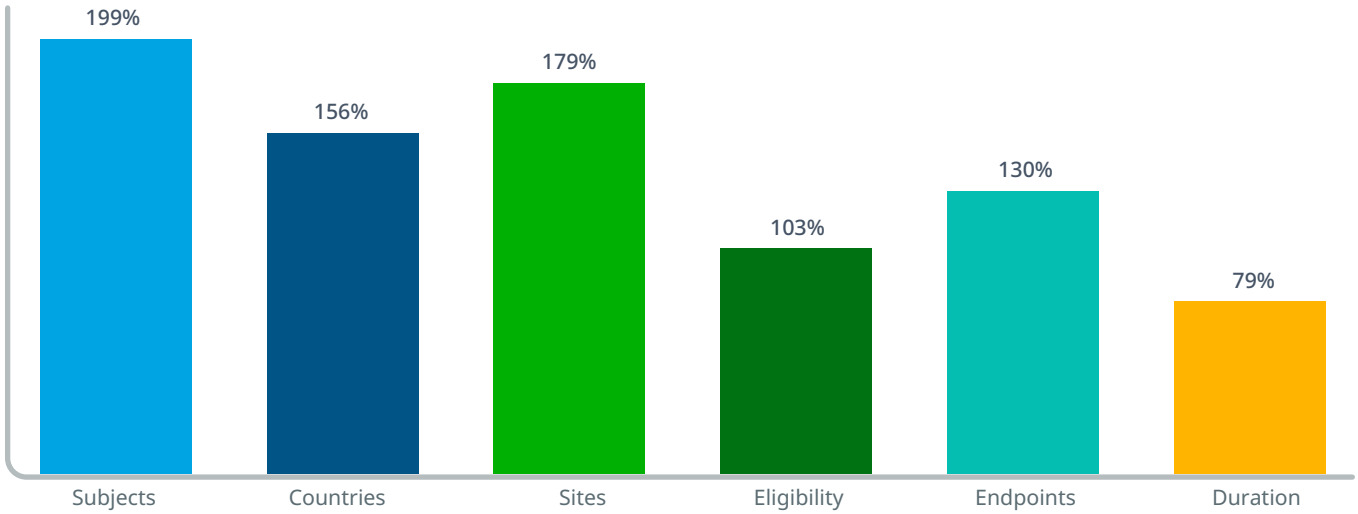
Source: Citeline Trialtrove, IQVIA Institute, Jan 2023.

- The relative discoverable use of remote, virtual or decentralized methods in clinical trials dipped in 2022 to return to 2019 levels after two years of COVID-19 pandemic associated increases.
- Early 2020 saw a sharp increase in reported decentralized methods that mirrored a sharp increase in total trial activity driven by COVID-19 therapeutic and vaccine development. This correlates with the critical nature of these methods as innovations that enabled trial continuity through the pandemic and record-breaking timelines in getting COVID-19 vaccines and therapeutics to patients.
- Despite the relative decrease in disclosed decentralized methods from the peak in 2021, the 2022 use of these methods is still at 2019 levels, where they first showed an elevation versus a relatively constant penetration over the previous nine years.

Notes: Trials which have a number of decentralized features often don't disclose those in trial registry information, and trials were identified as remote, virtual or decentralized based on a selection of words and phrases included in the trial description, design or notes and reflect an imperfect guide to trends in these trials. Some attributes considered are the use of words, phrases and synonyms as well exclusions for false positives. Generally, terms were similar to telemedicine, remote visits, use of remote sensors, or that the trial is noted to be remote, decentralized, siteless, virtual, or using the increasingly common use of electronic informed consent. In some cases central, remote or distributed are part of common medical terms associated with diseases and are unrelated to the trial design and were excluded. RVD analysis includes industry and non-industry, and interventional and non-interventional trials to enable identification of utilization trends.

RVD trials involve more subjects, sites, countries, and endpoints but have shorter durations than traditional trials

Exhibit 50: Phase II and III remote, virtual or decentralized trials (RVD) compared to traditional trial designs, 2010–2022



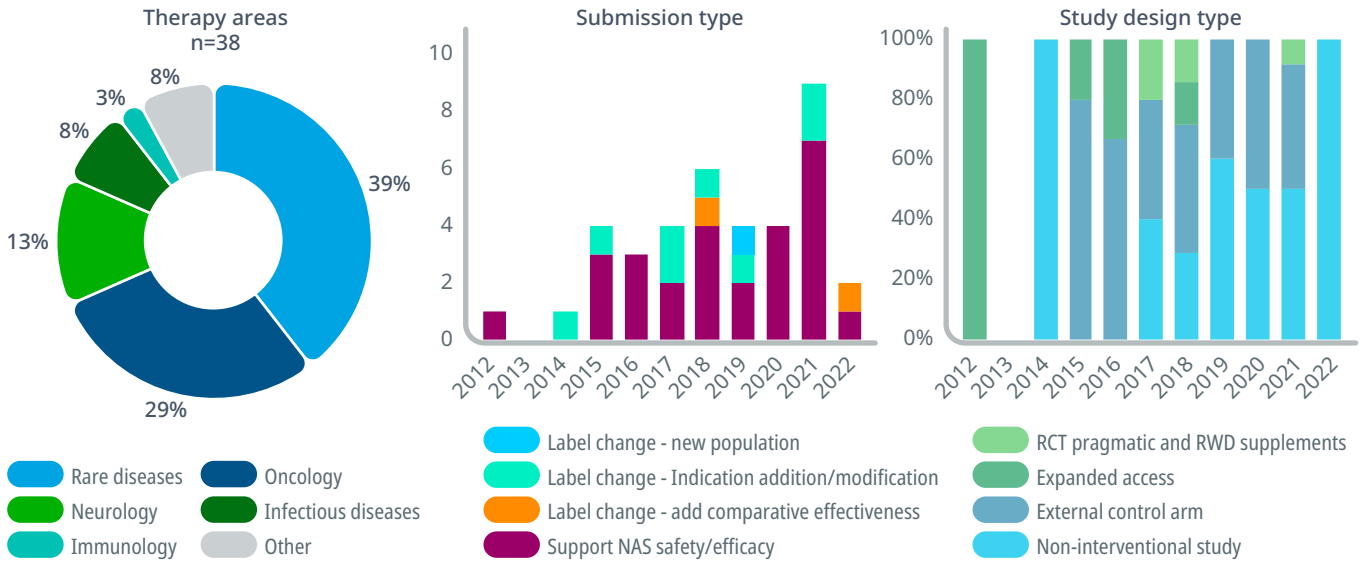
Source: Citeline Trialtrove, IQVIA Institute, Jan 2023.

- Analysis of a cohort of trials with disclosed use of remote, virtual or decentralized (RVD) methods demonstrates an increased level of complexity across key trial metrics, including number of subjects, countries, sites, eligibility criteria, and endpoints.
- Despite higher average complexity, the cohort of trials completed just over 20% faster than non-RVD trials.
- Specifically, analysis of the therapeutic split of trials with decentralized methodologies shows the highest number of trials in the analysis cohort coming from infectious disease, vaccines, immunology, and neurology. The heavy infectious disease and vaccines focus may partially account for the high number of subjects and the shorter average duration observed for the cohort, but the role of RVD in these therapeutically aligned differences is unclear.
- Many of the decentralized trial methodologies are being used in novel ways in hybrid trial settings, and the expectation is that as technology, processes, and system-wide experience with using these methodologies increases, complexity will be reduced.[8,9]

Notes: Trials which have a number of decentralized features often don't disclose those in trial registry information, and trials were identified as remote, virtual or decentralized based on a selection of words and phrases included in the trial description, design or notes and reflect an imperfect guide to trends in these trials. Some attributes considered are the use of words, phrases and synonyms as well exclusions for false positives Trial attributes from Citeline Trialtrove for the identified trials were compared to the 12-year cohort of all other trials that were not included in the novel design cohort. Includes industry interventional trials only. Excludes terminated trials.

The number of FDA approval decisions citing use of real-world evidence has been rising over the past decade but fell in 2022

Exhibit 51: FDA approvals based on real-world evidence (RWE), 2012–2022



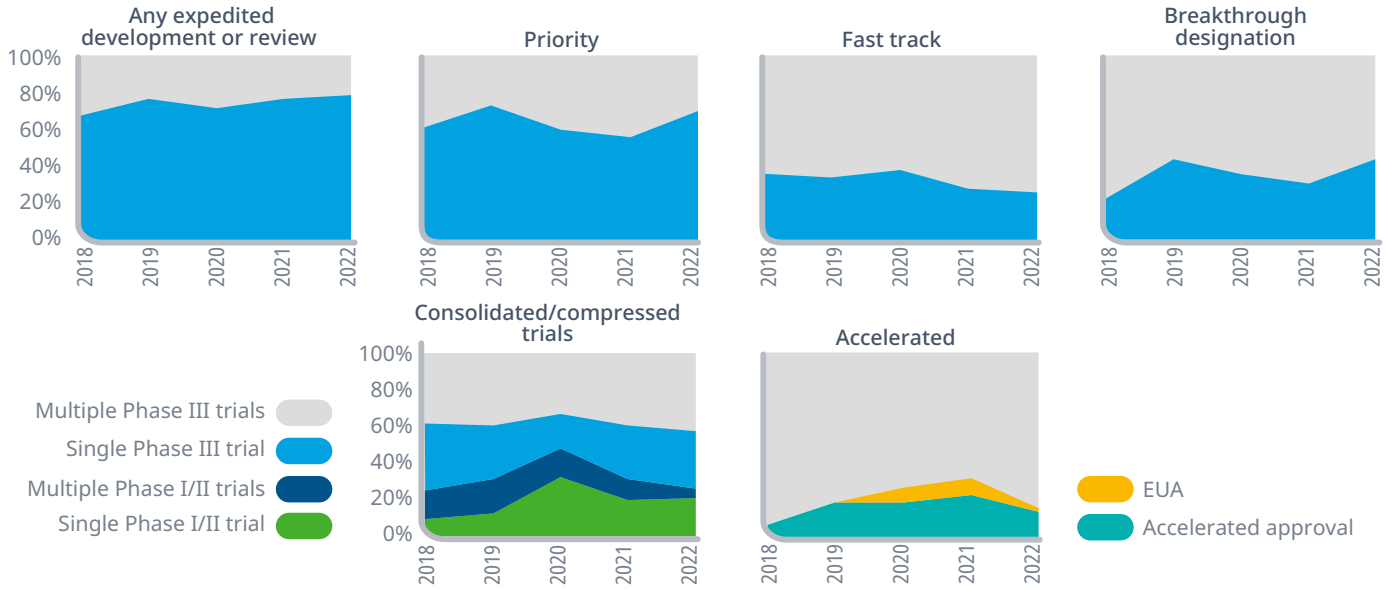
Source: Citeline Trialtrove, IQVIA Institute, Jan 2023.

- Over the past decade, RWE has been used in the U.S. in the new approval or expanded use of existing drugs 38 times, including two drugs in 2022.
- Over two-thirds of the approvals with RWE use in the past decade were associated with rare diseases and oncology approvals.
- 70% of these RWE submissions were used in support of NAS decisions, while 30% supported label changes, including supplementing with additional comparative effectiveness data, addition of a new patient population, or expansion to a new indication.
- Over the same time span, the predominant types of study design include use of external control arms (45% of the approvals) and non-interventional (e.g., observational) studies (40% of the approvals).
- While revised FDA guidance issued in December 2021 aims to shift RWE from being merely influential in the approval to a greater frequency of inclusion in the approval and/or findings referenced in package inserts, the decline in 2022 approvals based on RWE may be more representative of shifts in overall industry pipeline approvals away from oncology and rare diseases, and potential impact of increasing FDA focus on validating RWE use in supporting approval decisions.

Notes: Collected from public sources relating to the approval trials for medicines. Data collected under a treatment IND or expanded access protocol has been considered a form of RWE by the FDA, such as in rare disease settings where there is little chance of a prospective trial. RWE approvals shown here include those granted after approval (e.g., carglumic acid 2010 RWE but drug was a 2006 launch). Analysis includes some double counting where a drug may have had more than one type of RWE design type or submission type.

Most new drugs received expedited reviews with increases in priority and breakthrough designations in 2022

Exhibit 52: U.S. novel active substance (NAS) launches by characteristics of approval, 2018–2022



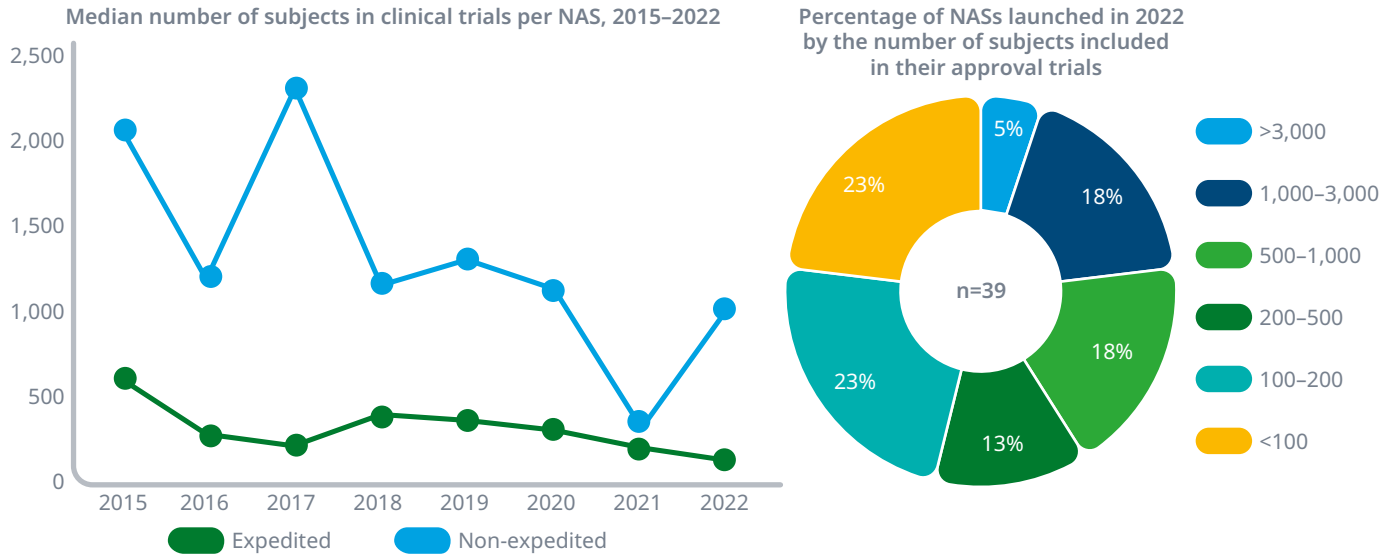
Source: IQVIA Institute, Jan 2023.

- In a continuing trend, increasing numbers of newly approved drugs have some form of expedited review in 2022, with 77% of the new launches being designated as priority, fast track, breakthrough or granted accelerated approvals.
- Of the 39 U.S. drugs launched in 2022, 26 had priority review, 16 were breakthrough designations, 10 were placed on the fast track pathway, and six were approved through accelerated approval — including one COVID-19 NAS with Emergency Use Authorization.
- Specifically, priority review and breakthrough designations rose in relative representation of U.S. NAS launches, while fast track and accelerated approval percentages dropped.
- Overall, in the past five years, the relative use of any expedited development or review mechanism as a percentage of total launches has increased by 15%.
- At the same time, use of consolidated trials remained stable, or decreased slightly, at least partially as a function of post-pandemic pipeline re-equilibration.

Notes: A novel active substance (NAS) is a new molecular or biologic entity or combination where at least one element is new; Includes NASs launched in the United States 2018-2022 regardless of the timing of FDA approval.

Recent approvals with forms of expedited review on average include relatively few patients

Exhibit 53: Number of subjects included in U.S. novel active substance (NAS) approval trials by review status and type



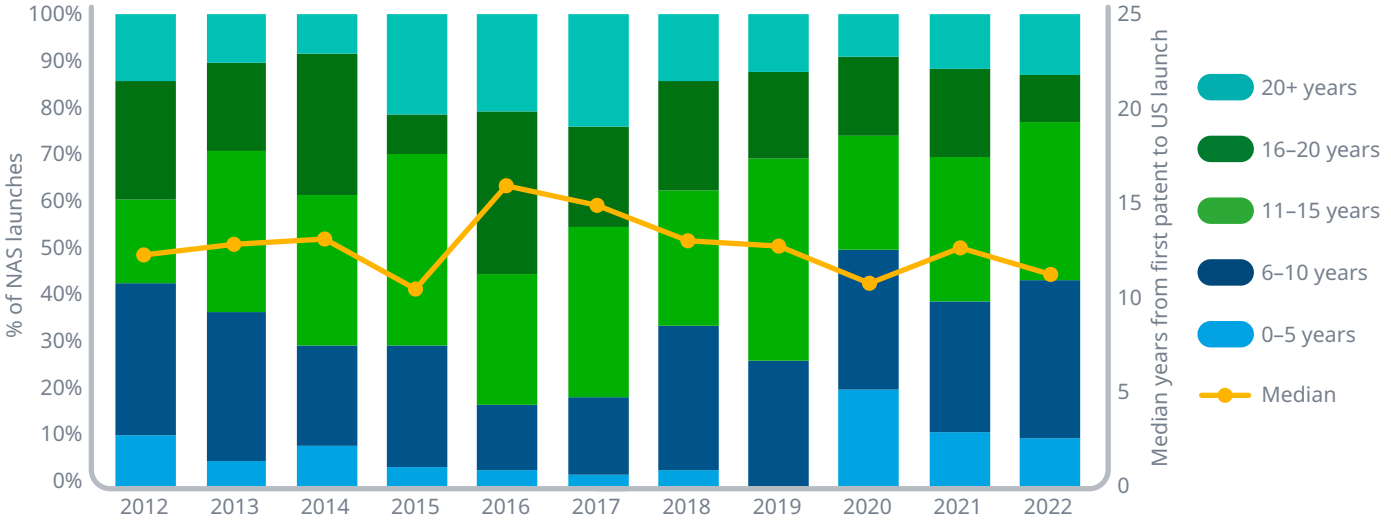
Source: IQVIA Institute, Jan 2023.

- The median number of patients enrolled in approval trials for 2022 launches with some form of expedited review was 15% that of trials for non-expedited launches.
- This has been the case for drugs launched between 2015–2022 where, on average, expedited median enrollment was 31% that of non-expedited.
- As the percent of expedited launches has steadily increased over the last five years (Exhibit 52), this has resulted in a steady pipeline-wide reduction in patients enrolled in approval trials, with a 55% reduction in median patient enrollment for all approval trials between 2018 and 2022 (not shown).
- While this analysis focuses on approval trials only and diverges from all trial analysis for RVD and NTD enrollment complexity, it does suggest that for successful clinical programs, productivity enablers and regulatory flexibility are yielding efficiencies where stakeholders see joint priority for the patient.

Notes: Expedited review includes accelerated approval, priority review, breakthrough therapy, and fast track designations, emergency use authorizations; orphan drug designation is not included as an expedited review but noted as it correlates with smaller numbers of trial subjects.

23 drugs were launched less than 5 years into their patent terms in the past 3 years, up from 15 in total from 2012–2019

Exhibit 54: Time from first patent filing and U.S. launch for novel active substances (NASs), 2012–2022



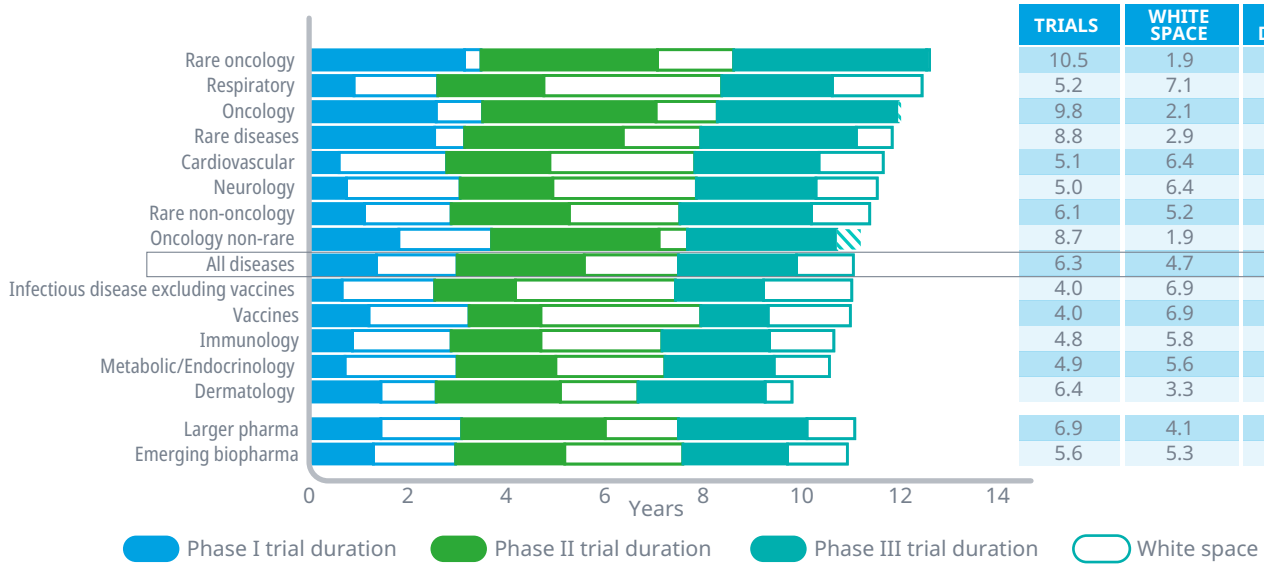
Source: IQVIA ARK Patent Intelligence, IQVIA Institute, Jan 2023.

- The time from when a company first patents an innovation to new medicine launch represents a useful proxy for the efficiency of the R&D process.
- The median time from first patent filing to launch for U.S. NAS remained near the lowest levels for the decade in 2022, at 11.2 years.
- Out of 39 launches in the U.S., four (10%) have less than five years from patent to U.S. launch, which includes one COVID-19 therapeutic, which received Emergency Use Authorization.
- Just over 30% of the 2022 launches were in the 6–10-year cohort — a slight increase over the previous year.
- Examination of drug approvals across the decade in the fastest cohort shows nearly all are targeting oncology or infectious disease.
- Looking at launches since 2017, 73% of the drugs launched in under 10 years included consolidated or compressed trials compared to 60% for all launches in the same time period.
- Only 29% of the launches in the fastest cohort were for first-in-class molecules compared to 42% for all launches since 2012, but in the next fastest launch cohort of 6–10 years, first-in-class molecules represented 42% of the drugs — on par with the full dataset, suggesting that while first-in-class does not necessarily carry a timing ‘penalty’ versus follow-on mechanisms, launches in the very fastest cohort are less frequently novel mechanisms.

Notes: Time is counted from the filing date of the first relevant patent, or the start of the first human trial whichever is earlier. Duration is calculated to the launch in the U.S, (not approval) determined through the appearance of sales volume in IQVIA audits or company statements indicating availability.

Some therapy areas have significantly shorter trial durations and 'white space' before starting a subsequent research phase

Exhibit 55: Comparison of trial duration to phase-change duration (years) in key disease areas, 2013–2022



	TRIALS	WHITE SPACE	TOTAL DURATION
Rare oncology	10.5	1.9	12.5
Respiratory	5.2	7.1	12.3
Oncology	9.8	2.1	11.9
Rare diseases	8.8	2.9	11.7
Cardiovascular	5.1	6.4	11.6
Neurology	5.0	6.4	11.4
Rare non-oncology	6.1	5.2	11.3
Oncology non-rare	8.7	1.9	11.1
All diseases	6.3	4.7	10.9
Infectious disease excluding vaccines	4.0	6.9	10.9
Vaccines	4.0	6.9	10.9
Immunology	4.8	5.8	10.6
Metabolic/Endocrinology	4.9	5.6	10.5
Dermatology	6.4	3.3	9.7
Larger pharma	6.9	4.1	11.0
Emerging biopharma	5.6	5.3	10.8

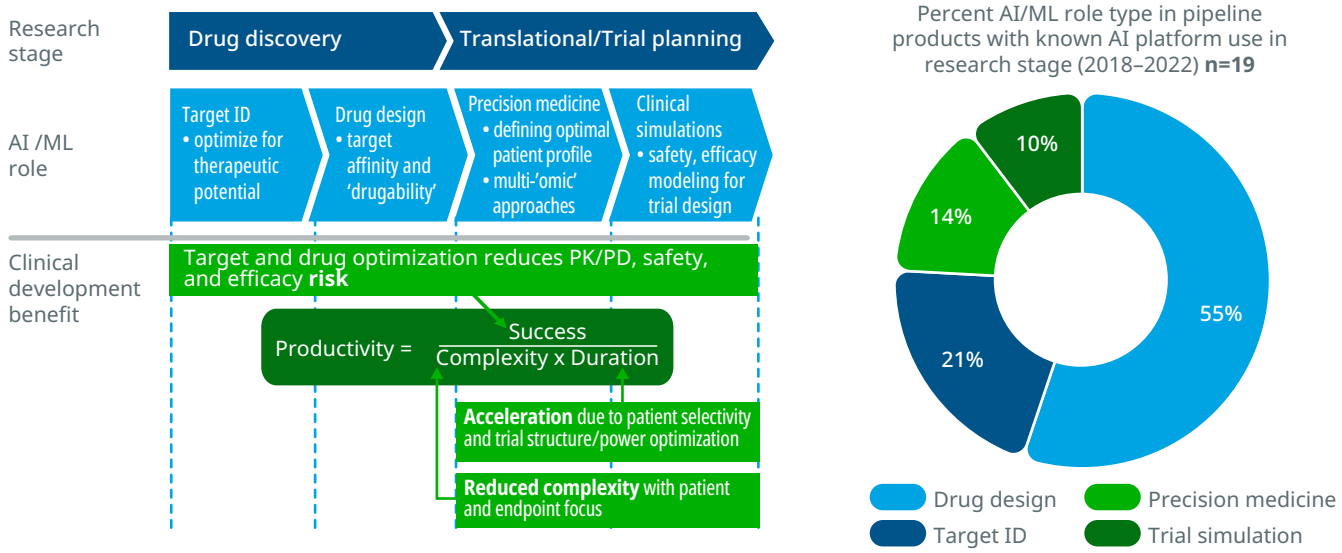
Source: IQVIA Pipeline Intelligence, Dec 2022; Citeline Trialtrove, IQVIA Institute, Jan 2023.

- Focus on total clinical program time and reducing 'white space' — the difference between the time a molecule takes to progress through clinical development and its clinical trial duration — remains a critical opportunity for improving clinical development productivity.
- On average, new drugs spend 43% of their development time on white space on the way to the patient.
- The proportion of white space varies widely across therapeutic areas, from 15% of total program duration for rare oncology to 63% for infectious disease and vaccines.
- While oncology has the shortest white space, it also has the longest treatment time, and the trade-off of treatment and white space timing is likely partially driven by high percentage of adaptive trials. Taking trial and white space time together, the total average program duration for oncology trials is longer than more than half of the remaining therapeutic areas.
- Comparison of large pharma and EBP shows very similar average program timing, but 30% longer white space timing for EBPs.
- These results speak to a complex interplay between white space, trial timing and total program timing. That said, in each therapeutic area, there are ongoing opportunities to optimize across all three.

Notes: Trial duration is counted from trial start to primary completion using Citeline Trialtrove. Phase duration is counted from phase start to subsequent phase start using IQVIA Pipeline Intelligence. The difference between these durations includes a variety of sponsor activities summarized for this analysis as 'white space'. Analyzed groups are not mutually exclusive.

Evidence of increasing potential for AI impact as research candidates advance into the clinical development pipeline

Exhibit 56: Impact of artificial intelligence (AI) on industry clinical development pipeline



Source: Clinicaltrials.gov, Citeline Trialtrove, IQVIA Institute, Jan 2023.

- Biopharmaceutical companies are applying AI/ML technology leveraging growing chemical, biological and patient datasets to accelerate and improve target and drug selection across the entire drug discovery continuum, with a set of most-used applications emerging.
- AI target selection by interrogating clinical, experimental, and 'omics' data to better characterize disease states and identify novel 'druggable' targets has been used in 21% of the AI/ML impacted molecules analyzed.
- Drug design represents the most common use of AI/ML in the assessed cohort, with 55% of analyzed products optimizing drug design by analyzing complex datasets, including molecule structure, molecular dynamics, genome, and combinatorial drug screening databases.
- The use of AI/ML to deliver insight from a range of patient 'omics,' biometrics and previous trial data to specifically optimize drug discovery through precision patient targeting is a focus for sponsor companies of 14% of the products in the analyzed cohort.
- Finally, trial simulation using AI/ML technologies on deep target, drug, and patient datasets is enabling optimized clinical trial design in 10% of the pipeline products analyzed.
- 2022 saw a 10-year peak of 11 trial starts for analyzed set of pipeline products with known AI/ML role in research and discovery stage (not shown). As this enabler matures, the expectation is that trials using AI/ML will deliver faster results at lower risk based on optimized drug characteristics and trial execution.

Notes: Not all AI/ML clinical pipeline activity is publicly disclosed and products with AI/ML activity in their research cycle were identified by searching for clinical trials that are sponsored or co-sponsored by companies with known focus on AI/ML research methodologies. Sponsors/co-sponsors whose clinical pipeline products were included in this analysis are: A2A Pharmaceuticals, AI Therapeutics, Aptuit, Auransa, BenevolentAI Bio, Berg Pharma/ BPGbio, Exscientia, Healx, Nimbus Therapeutics, PathAI, Pharos iBio, Recursion Pharmaceuticals Inc., Relay Therapeutics, Schroedinger, Silicon Therapeutics, Valo Health, and Verge Genomics. Each identified product may have more than one type of AI/ML role included in the analysis. This analysis does not include the use of AI/ML for clinical trial operations optimization including site and patient selection, or histology/pathology or end point analysis.

Notes on sources

THIS REPORT IS BASED ON THE IQVIA SERVICES DETAILED BELOW

ARK PIPELINE INTELLIGENCE is a drug pipeline database containing up-to-date R&D information on over 40,000 drugs, and over 9,000 in active development worldwide. The database captures the full process of R&D, covering activity from discovery stage through preclinical and clinical development, to approval and launch.

ARK PATENT INTELLIGENCE™ is a database of biopharmaceutical patents or equivalents in over 130 countries and including over 3,000 molecules. Research covers approved patent extensions in 51 countries, and covers all types of patents including product, process, method of use and others .

ARK NEW PRODUCT INTELLIGENCE is a database of over 500,000 products with distinct trade names, from launches dating back over 30 years covering over 60 major markets. The database reports on over 1,500 new launches every month, and the service provides insights on which companies are successful at launching products quickly, whether releasing a brand new chemical entity or the generic version of a drug that has lost patent protection.

IQVIA™ PHARMA DEALS is a comprehensive life science deals and alliances database that leverages worldwide information sources to deliver the latest intelligence in deals and alliances.

THIRD-PARTY INFORMATION

CITELINE'S TRIALTROVE provides intelligence about the drug development pipeline and information on clinical trials globally. Citeline reports that Trialtrove uses over 40,000 sources including ones in the public domain and is supported by experienced industry analysts. The database includes extracted information including protocol details, as well as additional industry-relevant search terms such as its proprietary patient segments, trial outcomes and biomarker tags. It includes information on trial design, eligibility criteria, endpoints, sites, sponsors as well as anticipated and actual start and end dates as available. These attributes have been leveraged extensively in the IQVIA Clinical Productivity Index. For more information on Trialtrove see www.pharmaintelligence.informa.com/clinical-trial-data

BIOWORLD is a suite of news services run by Clarivate which includes tracking and segmentation of biopharmaceutical funding deals including venture capital, IPO and follow-on financing and other public financing.

Methodologies

SUCCESS RATES

Using IQVIA Pipeline Intelligence, which includes event dates for a comprehensive range of drug development stages where disclosed or able to be determined by editorial staff, phase start dates were tracked for each product. A phase was considered successful if any subsequent phase has a later phase start date. In the absence of a subsequent phase start, the highest date for a negative event such as discontinuation, suspension, withdrawn by applicant, or inactive for greater than three years was examined. Analysis was conducted across all indications and considers success or failure at the drug level and so did not track a specific indication for each drug but rather measured the success of the overall program.

Overall, 32,300 distinct drugs were examined, for 129,200 potential phase transitions for events from 1977 to present. We then limited to products where the phase transitions completed between 2010 and 2022, with valid information regarding phase transitions, either successful or failed, which includes 9,625 distinct drugs and 13,926 phase transitions.

We consider the earliest date a drug entered each phase. We consider the latest date for negative event outcomes. Negative outcomes include discontinued, suspended and withdrawn which are noted in the data collection when the sponsor discloses it. Negative events also include inactivity which is determined when there is no verified activity for three years. Inactive records are assigned to the year inactivity was determined (last time record was active plus three years).

COMPLEXITY METRICS

Clinical trial data included in the complexity metrics — trial start and end dates, country locations, number of clinical sites, actual or target number of subjects, endpoints, and inclusion/exclusion criteria — rely on company reported information about ongoing or planned clinical trials. Substantial lags have been noted in the reporting of numbers of subjects, sites, and countries which all rely on site selection, startup, and recruitment and early trial information may not reflect the full extent of the effort required.

Historic evaluations of different year-end editions of this data indicate variation in the individual measures included in the complexity metric in the most recent year of data. In particular, the number of sites, countries, and subjects have shown significant variability in the numbers reported from one year to the next. Comparing across the year-end editions for 2020–2022, complexity metrics for average number of countries across all phases increased 13% in the latest year, sites increased 29%, and subjects increased 33%. These variations had an impact on overall complexity and productivity, increasing complexity in the most recently published year by 15% and decreasing productivity 6%.

Therefore, subjects, sites, and countries have been adjusted in the most recent year (2022) based on historic observations of this data latency. The most recent year is subject to change in subsequent periods.

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Murray Aitken is Executive Director, IQVIA Institute for Human Data Science, which provides policy setters and decisionmakers in the global health sector with objective insights into healthcare dynamics. He led the IMS Institute for Healthcare Informatics, now the IQVIA Institute, since its inception in January 2011. Murray previously was Senior Vice President, Healthcare Insight, leading IMS Health's thought leadership initiatives worldwide. Before that, he served as Senior Vice President, Corporate Strategy, from 2004 to 2007. Murray joined IMS Health in 2001 with responsibility for developing the company's consulting and services businesses. Prior to IMS Health, Murray had a 14-year career with McKinsey & Company, where he was a leader in the Pharmaceutical and Medical Products practice from 1997 to 2001. Murray writes and speaks regularly on the challenges facing the healthcare industry. He is editor of Health IQ, a publication focused on the value of information in advancing evidence-based healthcare, and also serves on the editorial advisory board of Pharmaceutical Executive. Murray holds a Master of Commerce degree from the University of Auckland in New Zealand, and received an M.B.A. degree with distinction from Harvard University.

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Nicole serves as Research Director for the IQVIA Institute for Human Data Science, leading Institute research focused on global pharmaceutical R&D-related topics. In this work, she partners with team members, IQVIA experts, and industry thought leaders to bring insights on R&D performance and ongoing innovation. Prior to joining the Institute in late 2021, she was Senior Director of R&D Strategy at IQVIA, where she partnered with the organization's leaders to frame corporate and therapeutic growth strategies. She also worked in the IQVIA Consulting organization from 2008 to 2014, leading projects with pharmaceutical and biotech clients and helping to optimize cross-functional drug development solutions. Before coming to IQVIA, Nicole worked in R&D organizational effectiveness at Pfizer, and began her career in 2008 in the Pharmaceutical and Medical Product practice at McKinsey & Company. Nicole holds a Ph.D. in Microbiology from Duke University and a B.S. in Biology from the State University of New York at Fredonia.

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Michael Kleinrock serves as Research Director for the IQVIA Institute for Human Data Science, setting the research agenda for the Institute, leading the development of reports and projects focused on the current and future role of human data science in healthcare in the United States and globally. Kleinrock leads the research development included in Institute reports published throughout the year. The research is focused on advancing the understanding of healthcare and the complex systems and markets around the world that deliver it. Throughout his tenure at IMS Health, which began in 1999, he has held roles in customer service, marketing, product management, and in 2006 joined the Market Insights team, which is now the IQVIA Institute for Human Data Science. He holds a B.A. degree in History and Political Science from the University of Essex, Colchester, UK, and an M.A. in Journalism and Radio Production from Goldsmiths College, University of London, UK.

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Thought Leadership Manager, IQVIA Institute for Human Data Science

Jamie Pritchett is Thought Leadership Manager for the IQVIA Institute, managing aspects of IQVIA Institute projects and conducting research and analysis within global healthcare. Prior to joining IQVIA in 2021, he held positions with the North Carolina Department of Health and Human Services and the Duke Human Vaccine Institute, where he developed skills in understanding and addressing the array of physical, environmental, and social contributors to individual health. Jamie uses his experience in public health, health communication, and drug development and research to understand current trends in healthcare and the life sciences industry.
He holds a Bachelor of Science in Animal Science and Zoology and a Master of Toxicology from North Carolina State University.

About the Institute

The IQVIA Institute for Human Data Science contributes to the advancement of human health globally through timely research, insightful analysis and scientific expertise applied to granular non-identified patient-level data.

Fulfilling an essential need within healthcare, the Institute delivers objective, relevant insights and research that accelerate understanding and innovation critical to sound decision making and improved human outcomes. With access to IQVIA's institutional knowledge, advanced analytics, technology and unparalleled data the Institute works in tandem with a broad set of healthcare stakeholders to drive a research agenda focused on Human Data Science including government agencies, academic institutions, the life sciences industry, and payers.

Research agenda

The research agenda for the Institute centers on five areas considered vital to contributing to the advancement of human health globally:

- Improving decision-making across health systems through the effective use of advanced analytics and methodologies applied to timely, relevant data.
- Addressing opportunities to improve clinical development productivity focused on innovative treatments that advance healthcare globally.
- Optimizing the performance of health systems by focusing on patient centricity, precision medicine and better understanding disease causes, treatment consequences and measures to improve quality and cost of healthcare delivered to patients.
- Understanding the future role for biopharmaceuticals in human health, market dynamics, and implications for manufacturers, public and private payers, providers, patients, pharmacists and distributors.
- Researching the role of technology in health system products, processes and delivery systems and the business and policy systems that drive innovation.

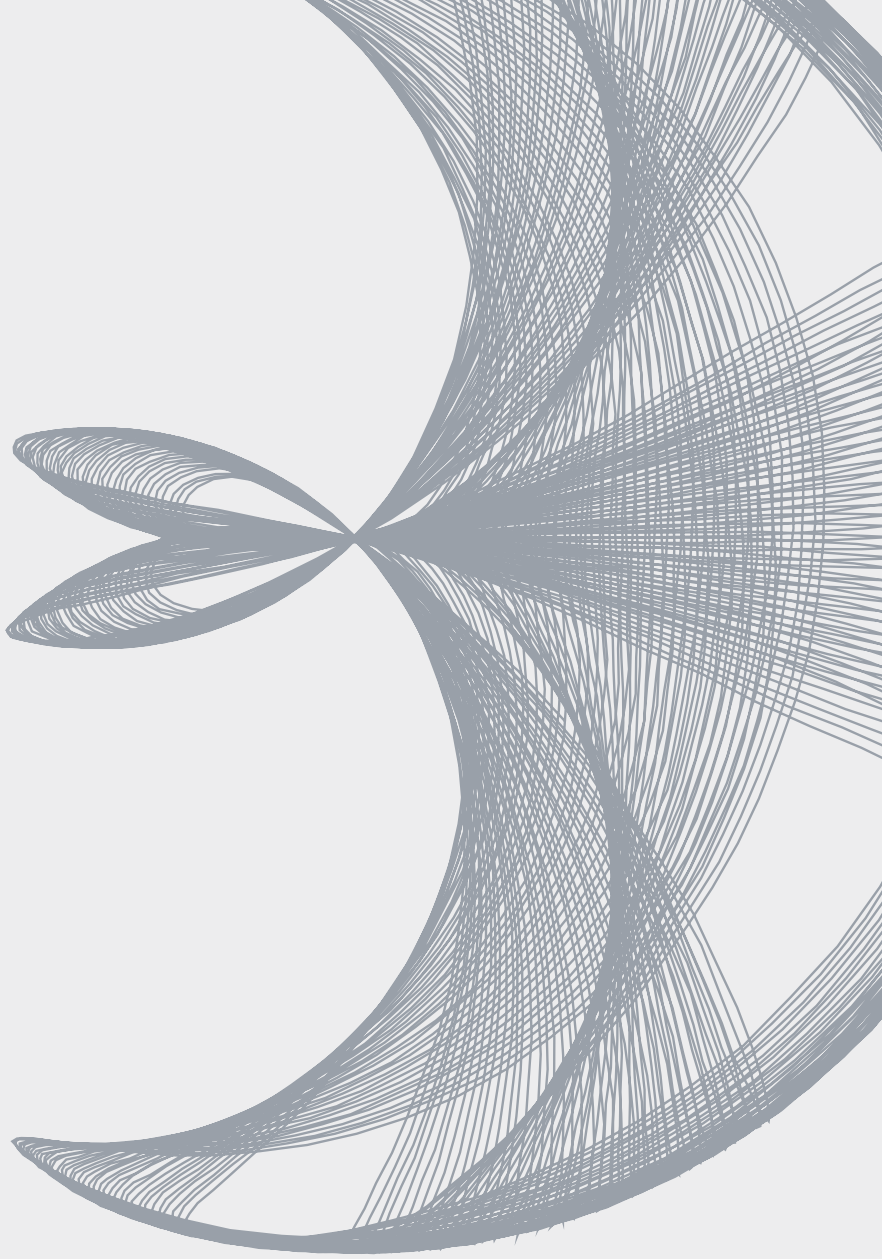
Guiding principles

The Institute operates from a set of guiding principles:

- Healthcare solutions of the future require fact based scientific evidence, expert analysis of information, technology, ingenuity and a focus on individuals.
- Rigorous analysis must be applied to vast amounts of timely, high quality and relevant data to provide value and move healthcare forward.
- Collaboration across all stakeholders in the public and private sectors is critical to advancing healthcare solutions.
- Insights gained from information and analysis should be made widely available to healthcare stakeholders.
- Protecting individual privacy is essential, so research will be based on the use of non-identified patient information and provider information will be aggregated.
- Information will be used responsibly to advance research, inform discourse, achieve better healthcare and improve the health of all people.

The IQVIA Institute for Human Data Science is committed to using human data science to provide timely, fact-based perspectives on the dynamics of health systems and human health around the world. The cover artwork is a visual representation of this mission. Using algorithms and data from the report itself, the final image presents a new perspective on the complexity, beauty and mathematics of human data science and the insights within the pages.

The algorithmic art featured in this report is generated using clinical development productivity attribute data, including the number of subjects, sites, endpoints, and eligibility criteria; trial durations; and success rates. These were collated for leading diseases over the period from 2010 to 2022.



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