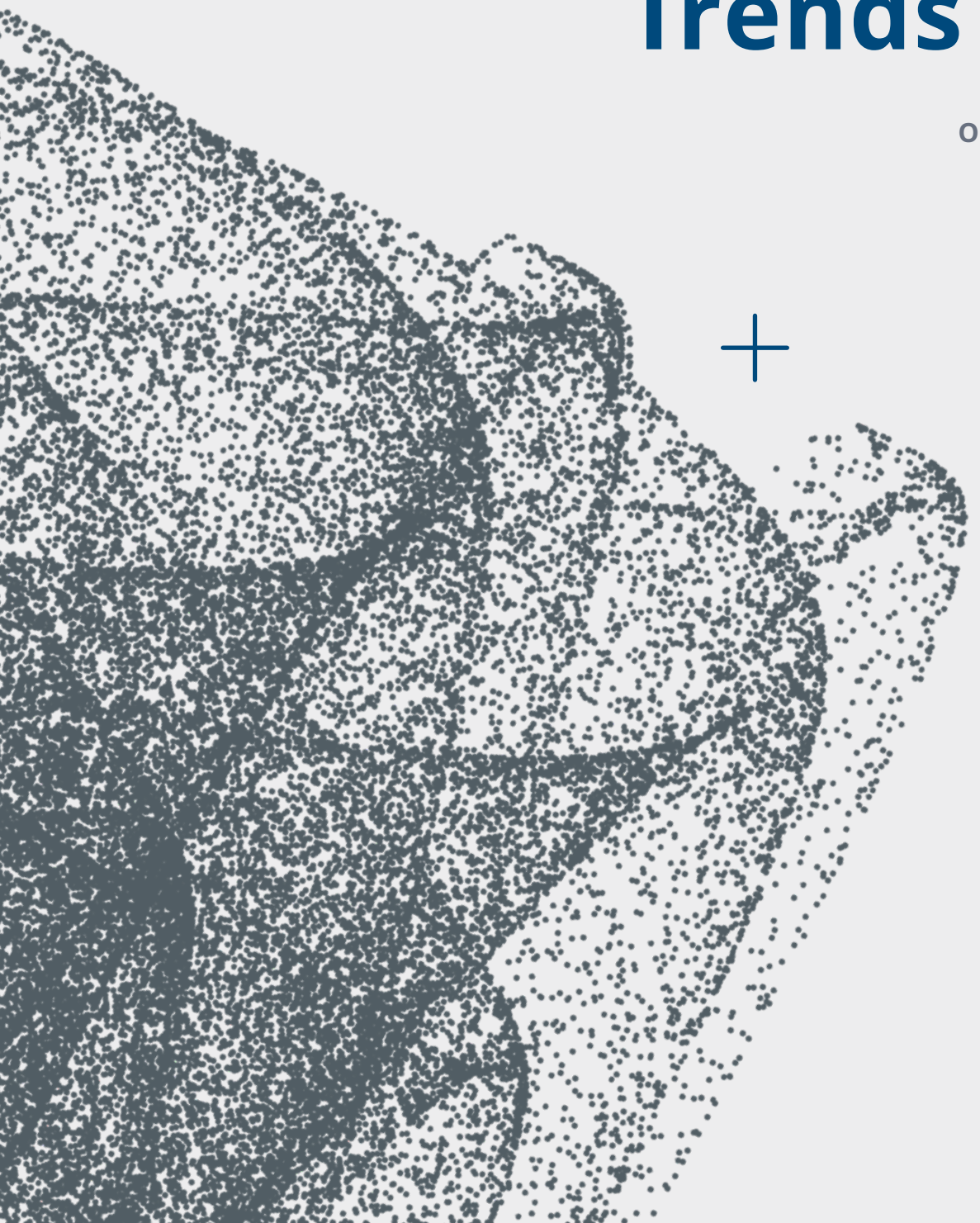
IQVIA INSTITUTE FOR HUMAN DATA SCIENCE

Global Oncology Trends 2022

OUTLOOK TO 2026



MAY
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Introduction

Oncology is the leading therapy area for innovation - in terms of the level of clinical trial activity, number of companies investing in therapeutics, size of the pipeline of therapies in clinical development, novel active substances being launched, and the level of expenditure on these drugs. In 2021, during a global pandemic, cancer care continued to be delivered although a backlog in treatment and screenings raised worrying questions. In a record-setting year, more novel cancer medicines became available for the first time than in any year in history, and many of them employ immunology or precision biomarkers to transform the way patients are treated. Adoption of breakthrough medicines and diagnostics is improving outcomes for millions around the world, though broad and equitable access remains a significant challenge to healthcare stakeholders — including patients.

This year's Global Oncology Trend report examines those novel medicines and the clusters of research, which promise a continuing sequence of breakthroughs in the decade to come. The report explores the impact of COVID-19 disruptions and the longer-term trends in the use of cancer medicines as well as the drivers of spending globally, in key geographies, by tumor type, and for specific types of oncology drugs.

The study was produced independently by the IQVIA Institute for Human Data Science as a public service, without industry or government funding. The contributions to this report of Caroline Anger, Priti Girotra, Natalie Harb, Kimberly Mehle, Shilpa Patyal, Chris Phelps, Tanya Partridge, Urvashi Porwal, Penny Price, Shivika Rastogi, Ivan Sebest, Durgesh Soni, Dan Winkelman, and dozens of others at IQVIA are gratefully acknowledged.

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MURRAY AITKEN
Executive Director
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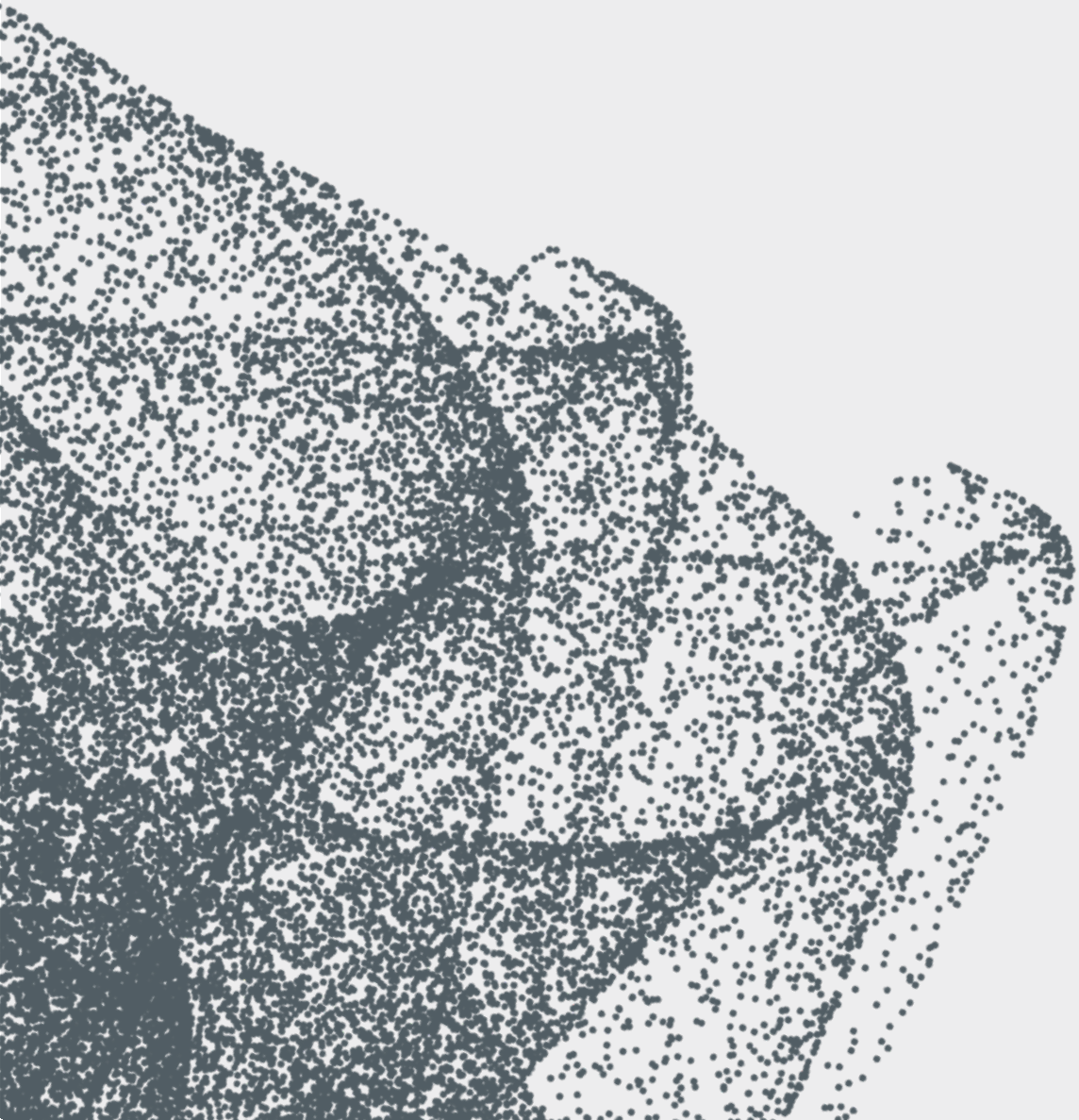
Table of contents



Executive summary

Global oncology is witnessing a remarkable surge in R&D and innovation, potentially leading to new therapies for unresolved cancers and including some of the most advanced breakthrough science in the life sciences. These therapies represent the largest area of collective research and the largest overall area by drug spending in the world. By contrast, the global oncology community and patients continue to struggle with the impact from delays in screenings, diagnoses and cancer care from COVID-19, as well as gaps in access and care which predated the pandemic. The outlook for the next five years includes important continuation of some of these trends and shifts in others.

NOVEL ACTIVE SUBSTANCES IN ONCOLOGY

A record 30 oncology novel active substances (NASs) were initially launched globally in 2021, 104 in the past five years and a total of 159 since 2012. While not all of these drugs have become available in every country, most have access to some key breakthroughs in immuno-oncology and the use of precision biomarkers have become the standard of care in dozens of tumors. In the U.S. there were 83 unique new cancer medicines launched in the past five years, with many approved for more than one indication. There have been important concentrations of new therapies in solid tumors of the lung, breast, prostate, and skin, as well as hematological malignancies such as non-Hodgkin's lymphoma and multiple myeloma. Many of these drugs are receiving accelerated approvals, orphan or breakthrough designations, and a small but increasing number are proceeding from patent filing to product launch in less than five years. As with most years in the past decade, new medicines launched in 2021 included significant clinical advances across a range of tumors and mechanisms.

The global oncology community and patients continue to struggle with the impact from delays in screenings, diagnoses and cancer care from COVID-19, as well as gaps in access and care which predated the pandemic.

ONCOLOGY RESEARCH AND DEVELOPMENT ACTIVITIES

Oncology trial starts reached historically high levels in 2021, up 56% from 2016 and mostly focused on rare cancer indications, which have higher success rates despite greater complexity. Most cancer research focuses on metastatic or advanced cancers, but early cancer and vaccines have more than doubled in 10 years and represent a steady 11% of trials.

Compared to other therapy areas, oncology trials have significantly higher complexity measured in numbers of eligibility criteria, endpoints, trial sites, countries, and clinical subjects. Oncology also shows among the lowest "white space" — the difference between the duration of clinical trials and the duration of time between trial phases when administrative activities often take place — ultimately accelerating successful drugs time to the market. Composite success rates in oncology have been trending down since 2015, reaching 5.2% in 2021, while rare tumors averaged 15.6%. Combining probability of success with complexity and duration, overall productivity of oncology research is among the lowest in the industry, though rare cancer productivity is high and is rising steadily.

In terms of the sponsors of research, emerging biopharma companies were responsible for 68% of the oncology pipeline in 2021, up from 45% a decade ago, and increasingly involved without larger pharma company partners until later in the development of an asset, or even after it has launched. Notably, some emerging companies headquartered in China have succeeded in getting approval for novel drugs in the U.S.

There has been a steady rise in the number of companies from China sponsoring research and many of them will likely partner with multinationals to reach developed markets. Even with such arrangements, recent setbacks with FDA suggest that these emerging companies may not have designed trials to meet the expectations of developed market regulators.

IMPACT OF COVID-19 ON CANCER CARE

Oncologists are reporting caseloads are 20–29% below pre-COVID-19 levels and more new patients presented to community oncologists with metastatic disease in several tumors during 2020 and 2021. After two decades of innovation driving improved outcomes across solid and hematological tumors, these setbacks in engagement, screening and prevention are worrying providers and policymakers. Even as disruption to cancer care eases with the pandemic shifting into a new phase, delays in surgeries, chemotherapy and fewer diagnoses being conducted continue to be a concern for oncologists. Screenings for common cancers were down 1–16% in the U.S. through the end of 2021. More than 30 million screenings for four common tumors have been disrupted since the onset of the pandemic, risking delayed or missed diagnoses for more than 58,000 patients.

CANCER PATIENT ACCESS AND USE OF SCIENTIFIC ADVANCES

The number of treated cancer patients globally grew at an average of 4% over the past five years and is expected to accelerate in the next five years as COVID-19 disruptions ease. Despite this growth, the pace of bringing novel cancer therapies to patients is uneven across countries, with differences in biomarker testing rates, adoption of novel therapies, and the presence of infrastructure capacity to deliver some of the most advanced therapies. While some biomarkers are tested similarly across countries, others have wide differences, which influence the medicines that are used. Use of checkpoint inhibitors is two to three times higher in some major developed countries than others and is much higher than in lower income countries.

Non-small cell lung cancer treatment has shifted to include checkpoint inhibitors as the standard of care in the past three years, contributing to the extension of the median duration of first-line therapy by almost half a year, and yet lower income countries with the least access often have the highest persistent rates of smoking in the world. Melanoma is treated with immuno-oncology checkpoint inhibitors 80% of the time with rising use of combo regimens, bringing significant life extension for metastatic patients. Next-generation biotherapeutics, including cell and gene therapies, are an area of intense research, and while the number of CAR T centers is growing, locations are generally not convenient to all patients and not all centers have all approved products available, potentially resulting in lack of access to patients without the resources to travel longer distances.

SPENDING ON ONCOLOGY MEDICINES

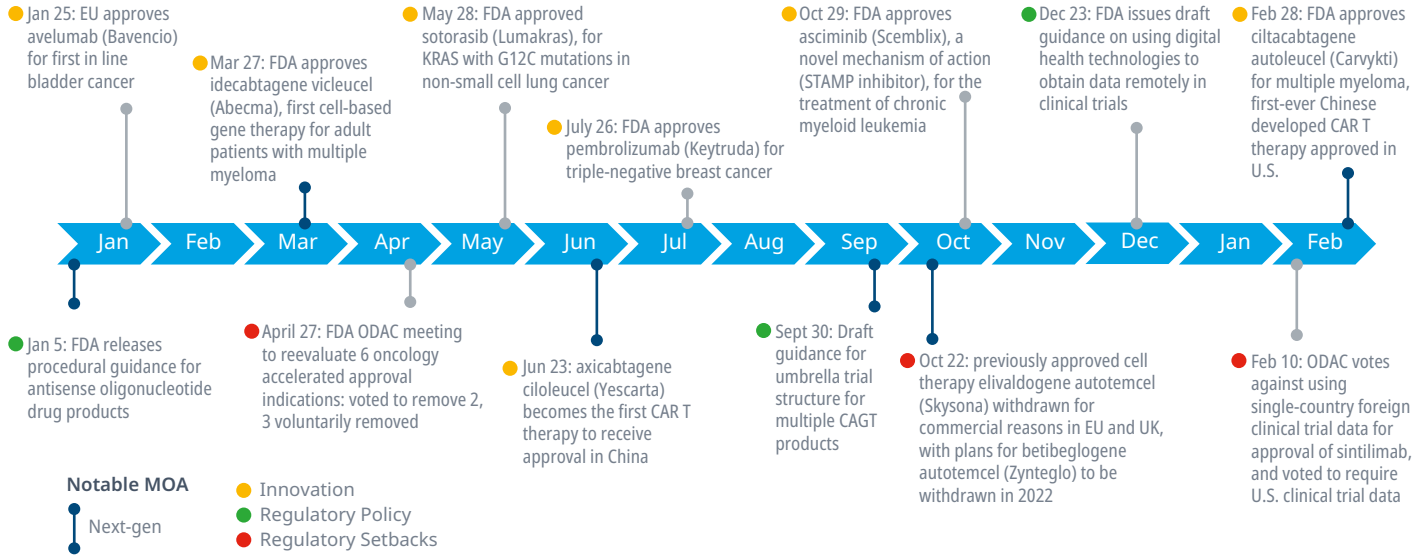
Cancer medicine spending rose to $185Bn globally in 2021 and is expected to reach more than $300Bn by 2026, driven by continued innovation. Growth in major markets is driven by new products and brand volume and offset by losses of exclusivity, including biosimilar impact. The U.S. remains the largest market globally followed by major countries in Europe. China oncology spending now exceeds the rest of pharmerging countries, driven by expanded access to new therapies and offset by lower prices. Globally, seven of the top ten tumors will see double digit spending growth from expected novel therapies. Together, PD-1/L1 inhibitors are used across most solid tumors and represent 45% of spending for lung cancer in 2021. The robust pipeline of next-generation biotherapeutics in oncology includes significant potential as well as a wide range of uncertainty both clinically and commercially, with a potential to lift the current $3Bn global spending to $15Bn by 2026 or as high as $40Bn in optimistic scenarios.

Novel active substances in oncology

- A number of significant events have occurred in oncology since January 2021, with important implications for drug development.
- A record 30 oncology novel active substances (NASs) were initially launched globally in 2021, and a total of 159 have been launched since 2012.
- A total of 104 oncology NASs have launched globally in the past five years, bringing the 20-year total to 215.
- In the U.S. there were 83 unique new cancer medicines launched in the past five years, with many approved for more than one indication.
- The median time from patent filing to product launch for the 2020 NAS cohort for oncology products fell to 8.5 years in 2021.
- Oncology drugs increasingly receiving accelerated approvals, orphan or breakthrough designations.
- The EMA approved six small molecule and four biologic NASs for oncology in 2021, fewer than the 14 total approved in 2020.
- Since 2011, 96 NASs were launched in the U.S. to treat solid tumors, with some approved for multiple indications.
- In the U.S., there were 55 unique new hematological cancer medicines launched since 2011.
- New medicines launched in 2021 included significant clinical advances across a range of tumors and mechanisms.

A number of significant events occurred in oncology since January 2021 with important implications for drug development

Exhibit 1: Notable events in drug approvals and regulatory action



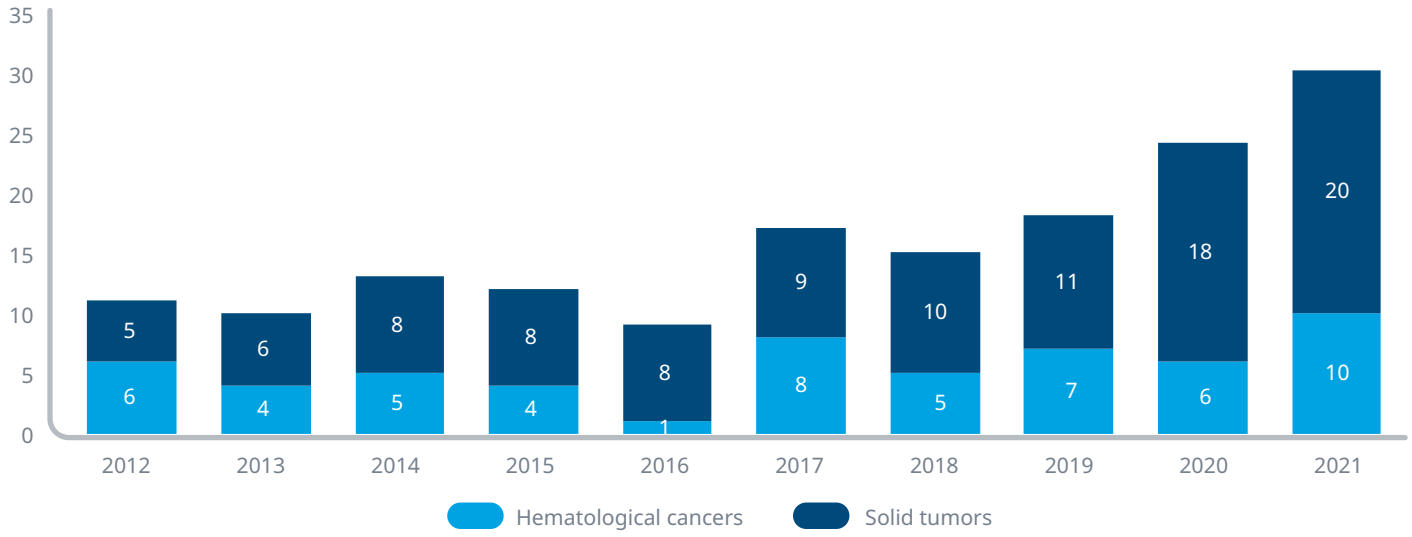
Source: IQVIA Institute, Apr 2022.

- 2021 and the beginning of 2022 saw significant events in oncology innovation, regulatory decisions and guidance from the FDA.
- Next-generation biotherapeutics continue to be important in oncology with an increasing focus on chimeric antigen receptor (CAR) T-cell therapies. FDA approved idecabtagene vicleucel (Abecma) and ciltacabtagene autoleucel (Carvykti) for multiple myeloma. Carvykti became the first Chinese developed CAR T therapy to be approved in the U.S. Additionally, axicabtagene ciloleucel (Yescarta) became the first CAR T therapy approved in China, highlighting the increasing role of China in research and development.
- In April last year, FDA requested the Oncologic Drugs Advisory Committee (ODAC) re-evaluate accelerated approval indications for PD-1/L1 checkpoint inhibitors. In total, nine accelerated approval indications were withdrawn or revoked for PD-1/L1 checkpoint inhibitors in 2021, with most of these voluntarily withdrawn by companies prior to or following the ODAC meeting. By contrast, checkpoint inhibitors are still approved for dozens of other indications that have not been withdrawn or revoked.
- ODAC also highlighted the importance of U.S. clinical trial data in the review of sintilimab, a Chinese developed checkpoint inhibitor, which it rejected for several reasons, including having China-only clinical trial data and being unrepresentative of the U.S. population as well as the trial lacking FDA site inspections.

Notes: Information collated from public sources including FDA, EMA and company press releases.

A record 30 oncology novel active substances (NASs) were initially launched globally in 2021, with 159 total since 2012

Exhibit 2: Global oncology launches of novel active substances (NAS), 2012–2021



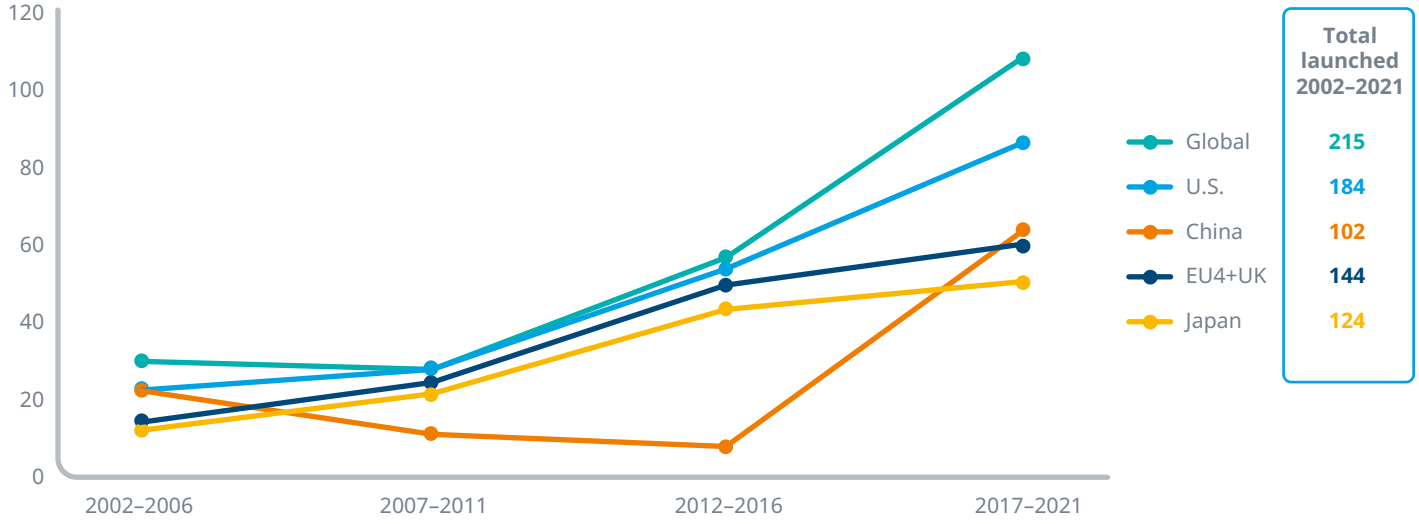
Source: IQVIA Institute, Apr 2022.

- A record 30 novel active substances (NASs) for oncology were launched globally in 2021.
- While the number of NASs launched for oncology globally averaged 11 each year from 2012–2016 — and averaged just 5 the five years prior — this has grown to an average of 21 new oncology launches each year from 2017–2021 and is steadily trending upward.
- Two-thirds of oncology NAS launches have been for solid tumors in recent years, with 68 launches for solid tumors in the last five years, up from 35 in the five years prior.
- While a majority of the innovation has been in solid tumors, hematological cancers continue to see increased innovation, with 36 NASs launched for hematological cancers in the last five years, up from 20 in the five years prior.
- Many of the NAS launched have multiple indications, further increasing the number of patients who may benefit from these novel compounds.

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. Oncology includes diagnostics.

A total of 104 oncology NASs have launched globally in the past 5 years and 215 over 20 years, with large geographic variations

Exhibit 3: Number of oncology novel active substances launched globally and in selected countries



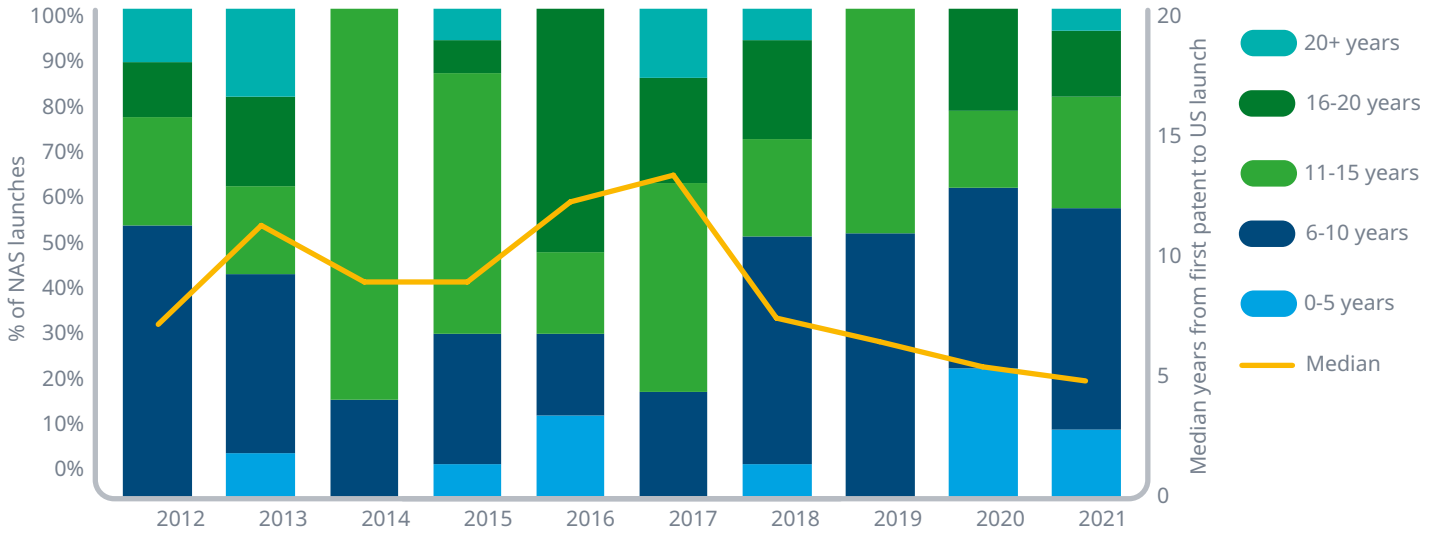
Source: IQVIA Institute, Apr 2022.

- Globally, 215 NASs have launched to treat cancers in the last 20 years, with nearly half of these (104) in the last five years.
- The U.S. has seen 83 NAS launches for oncology in the last five years, with 184 over the last 20 years, and has consistently been first to launch the majority of cancer medicines worldwide.
- Notably, 21 global NASs launched in the last five years have not launched in the U.S., and all but two were first launched in China or Japan, suggesting the emergence of divergent sources and destinations of innovation.
- EU4+UK has had 58 oncology NASs launched in the last five years and 144 over the 20-year period, with 31 of those launched in the U.S. during 2017-2021 not yet approved in Europe.
- China had 61 oncology NASs launched in the most recent five-year period compared to 41 from 2002–2016. This is likely driven by regulatory acceleration mechanisms from the National Medical Products Administration (NMPA) to bring both domestic and foreign developed drugs to Chinese citizens faster.
- Of the 61 NASs launched in China during 2017–2021, 14 have only been launched in China and only three of these have no development activity outside of China.

Notes: A novel active substance (NAS) is a new molecular or biologic entity or combination where at least one element is new and is noted in the year it launches for the first time in the relevant geography. Oncology includes diagnostics.

8 oncology drugs were launched less than 5 years into their patent terms in the past 2 years, up from 4 in total from 2012–2019

Exhibit 4: Time from first patent filing and U.S. launch for novel active substances (NASs), 2012–2021



Source: IQVIA ARK Patent Intelligence, IQVIA Institute, Apr 2022.

- The time between the first patent filing for a drug and the launch into the market represents an important assessment of the amount of protected life remaining when a product launches.
- As some accelerated approval pathways shorten approval times, this measurement of elapsed time provides insight into whether the acceleration changes these other dynamics of a product's lifecycle.
- The median patent to launch for the 2021 oncology NAS cohort was 8.5 years and is the shortest since 2007.
- The median patent to launch has declined significantly for oncology products launched in recent years, from a peak median patent to launch time of nearly 15 years in 2017.
- Sixty-one percent of oncology NASs launched in 2020 and 2021 had patent to launch times less than 10 years, with 20% less than five years.

Notes: For each novel active substance (NAS) launched, the first patent filing was researched to determine the time difference. The patent is not necessarily the binding patent that determines loss of exclusivity but represents the first time the sponsor deemed the innovation worthy of filing. Oncology includes diagnostics. Time from first patent filing to launch relates to the first indication(s) regardless of the future withdrawal or revocation of those indications. None of the withdrawn indications (see exhibit 1) were first indications for the relevant products.

There were 20 new cancer medicines and 2 cancer diagnostic agents, with 16 that were orphan designate

Exhibit 5: Oncologic novel active substances launched in the U.S. in 2021

*ATTRIBUTES KEY: 1 = Oral 2 = Recombinant 3 = Orphan 4 = First-in-class 5 = Accelerated approval 6 = RWE 7 = U.S. Patent to launch <5 years

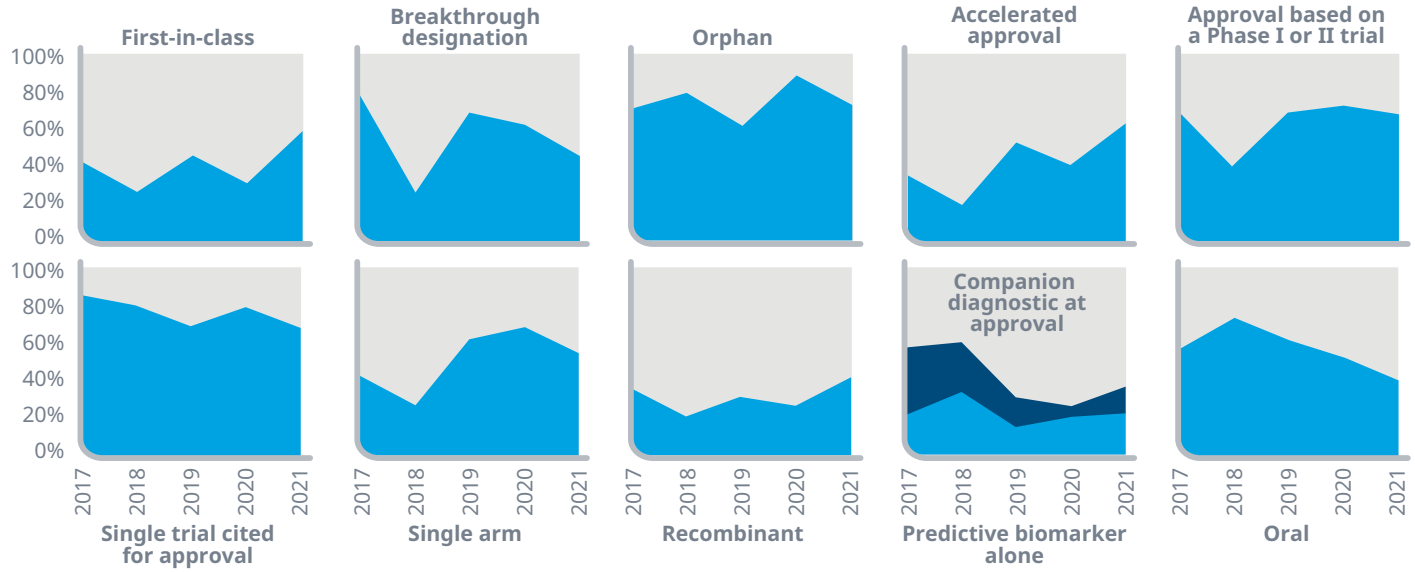
THERAPY AREA	INDICATION	MOLECULE	BRAND	ATTRIBUTES*						
				1	2	3	4	5	6	7
Oncology	Acute lymphoblastic leukemia (ALL) + Lymphoblastic lymphoma (LBL)	asparaginase erwinia chrysanthemi (recombinant)	Rylaze		●	●		●		●
	Bone marrow suppression	trilaciclib	Cosela			●	●		●	
	Cervical cancer	tisotumab vedotin	Tivdak		●		●	●		
	Cholangiocarcinoma with fibroblast growth factor receptor 2 (FGFR2) mutation	infigratinib	Truseltiq	●		●		●		
	Chronic myelogenous leukemia	asciminib hydrochloride	Scemblix	●		●	●	●		
	Endometrial cancer	dostarlimab	Jemperli		●			●		
	HER2-positive + breast cancer	margetuximab	Margenza		●	●				
	Large b-cell lymphoma	lisocabtagene maraleucel loncastuximab tesirine	Breyanzi Zynlonta		● ●	● ●	● ●	● ●		
	Marginal zone lymphoma and follicular lymphoma	umbralisib	Ukoniq	●		●	●	●		
	Multiple myeloma	melphalan flufenamide idecabtagene vicleucel	Pepaxto Abecma		●	● ●	● ●	● ●	●	●
	Neuroblastoma	naxitamab	Danyelza		●	●		●		
	Non-small cell lung cancer (NSCLC) with EGFR exon 20 insertion mutations	amivantamab mobocertinib	Rybrevant Exkivity	●	●	● ●	● ●	● ●		
	Non-small cell lung cancer (NSCLC) with KRAS G12C mutations	sotorasib	Lumakras	●		●	●	●	●	●
	Non-small cell lung cancer (NSCLC) with MET exon 14 skipping alterations	tepotinib	Tepmetko	●		●				
	Prostate cancer	relugolix	Orgovyx	●						
	Renal cell carcinoma	tivozanib	Fotivda	●						
	Von hippel-lindau (VHL) disease with associated renal cell carcinoma (RCC), hemangioblastomas, or pancreatic neuroendocrine tumors (PNET)	Belzutifan	Welireg	●		●	●			
Diagnostics	Ovarian cancer imaging	pafolacianine	Cytalux			●	●			
	Prostate cancer imaging	piflufolastat F 18	Pylarify							
Totals				9	9	16	13	14	3	3

Source: IQVIA Institute, Apr 2022.

- Twenty-two oncology novel active substances were launched in the U.S. in 2021 across a variety of solid tumors and hematological cancers, including two diagnostic agents.
- Sixteen of these NASs launched with orphan drug designations and 13 were first-in-class, indicating a focus on new mechanisms of action to treat rare cancers.
- Nearly half were oral medications that may be easier to administer outside of a hospital or clinic, a benefit for cancer patients but involving different patient cost-sharing models, depending on the patient's insurance.
- Sixty-four percent were approved through accelerated approval and will require further confirmatory clinical trials before conversion to standard approval.

Oncology drugs increasingly receiving accelerated approvals, orphan designations and are approved based on early trials

Exhibit 6: U.S. oncology NAS launches by characteristics of approval, 2017–2021



Source: IQVIA Institute, Apr 2022.

- New launches in the past six years have demonstrated diverse trends across specialized attributes relating to their novelty, form, approval pathway, and nature of evidence.
- Most of the discovery and development of new oncology medicines in recent years has focused on patients with rare cancers where few, if any, treatments may already exist, and 76% of NAS launches in the last five years received one or more orphan designations.
- Drugs which were the first-in-class using a novel mechanism represent an increasing share of NAS launches in oncology, with 59% in 2021 and 42% in the last five years.
- Increasingly, oncologics are approved through accelerated approval, with 64% of 2021 NAS launches approved this way, up from 36% in 2017.
- Many of the medicines over the past five years have been approved based on relatively limited trial evidence, in single trials with a single study arm, and based on their demonstrated evidence in earlier phase trials.
- The number of new oncologics administered orally has been declining, with 41% of the launches in 2021 and 55% in the last five years, an aspect that influences the setting in which they can be administered and the type of insurance benefit that covers them.

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 U.S. 2017–2021 regardless of the timing of FDA approval. Oncology includes diagnostics. Orphans include drugs with one or more orphan indications approved by the FDA at product launch. Products are not reclassified in this analysis as orphan if they subsequently receive an approval for an orphan designated indication after the launch year.

The EMA approved 6 small molecule and 4 biologic NASs for oncology in 2021, fewer than the 14 total approved in 2020

Exhibit 7: EMA approval trends for oncologic NASs approved for the first time in 2021

***ATTRIBUTES KEY:** 1 = Oral therapy 2 = Predictive biomarker 3 = Approval based on a Phase I or II trial, 4 = Single arm 5 = Multi-indication at approval 6 = Orphan 7 = Conditional marketing authorization

THERAPY AREA	INDICATION	BRAND	MOLECULE	ATTRIBUTES*						
				1	2	3	4	5	6	7
Small molecules	Breast neoplasms, neoplasm metastasis	Tukysa	tucatinib	●		●				
	NSCLC, thyroid neoplasms	Retsevmo	selpercatinib	●		●	●	●		●
	Cholangiocarcinoma	Pemazyre	pemigatinib	●	●	●	●		●	●
	CLL, follicular lymphoma	Copiktra	duvelisib	●		●	●			
	AML	Onureg	azacitidine							
	Multiple myeloma	Nexpovio	selinexor	●		●	●			●
Biologics	Breast neoplasms	Enhertu	trastuzumab deruxtecan		●	●	●			●
	Endometrial neoplasms	Jemperli	dostarlimab		●	●				●
	Hairy cell leukemia	Lumoxiti	moxetumomab pasudotox				●		●	
	Blastic plasmacytoid dendritic cell neoplasm (BPDCN)	Elzonris	tagraxofusp			●	●		●	
Totals				5	3	8	7	1	3	5

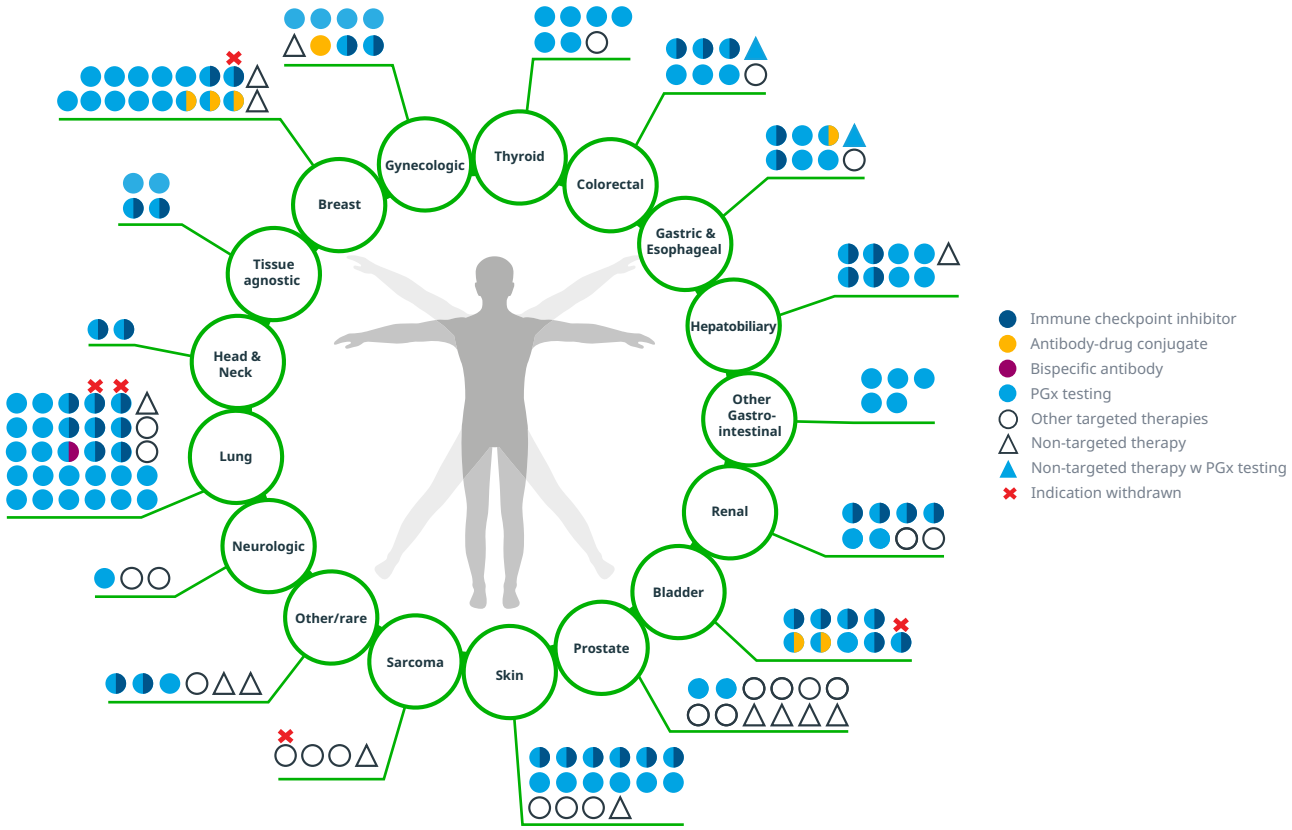
Source: IQVIA Institute, Apr 2022.

- There were 10 new oncology drugs approved by the EMA in 2021, fewer than the 14 approved in 2020.
- Only three were associated with predictive biomarkers, including dostarlimab (Jemperli) a PD-1 checkpoint inhibitor, and trastuzumab deruxtecan (Enhertu), an antibody-drug conjugate targeting HER2-positive breast cancer.
- Five out of ten approvals are small molecules administered orally, reducing the need for specialty visits for IV infusions.
- Only three were developed to address rare cancers, notably different from the U.S. launches where nearly all received orphan designation.
- Nearly all (8 of 10) were approved based on earlier phase trials, and half are conditional marketing authorizations. EMA has noted that these authorizations require further data post-approval to convert to full approvals and have balanced the unmet need of patients with the benefit to patients of the immediate availability of the new treatments.
- With the robust numbers of ongoing clinical trials, along with rising numbers of approved treatments essentially competing for patients, the scarcity of eligible patients is becoming a factor for sponsors and regulators to balance in determining the risks and benefits of novel drugs.

Notes: AML=acute myeloid leukemia; NSCLC=non-small cell lung cancer; CLL=chronic lymphocytic leukemia.

Since 2011, 96 NASs were launched in the U.S. to treat solid tumors, with some approved for multiple indications

Exhibit 8: U.S. NASs in solid tumors launched 2011–2021 with indications including those granted after initial launch



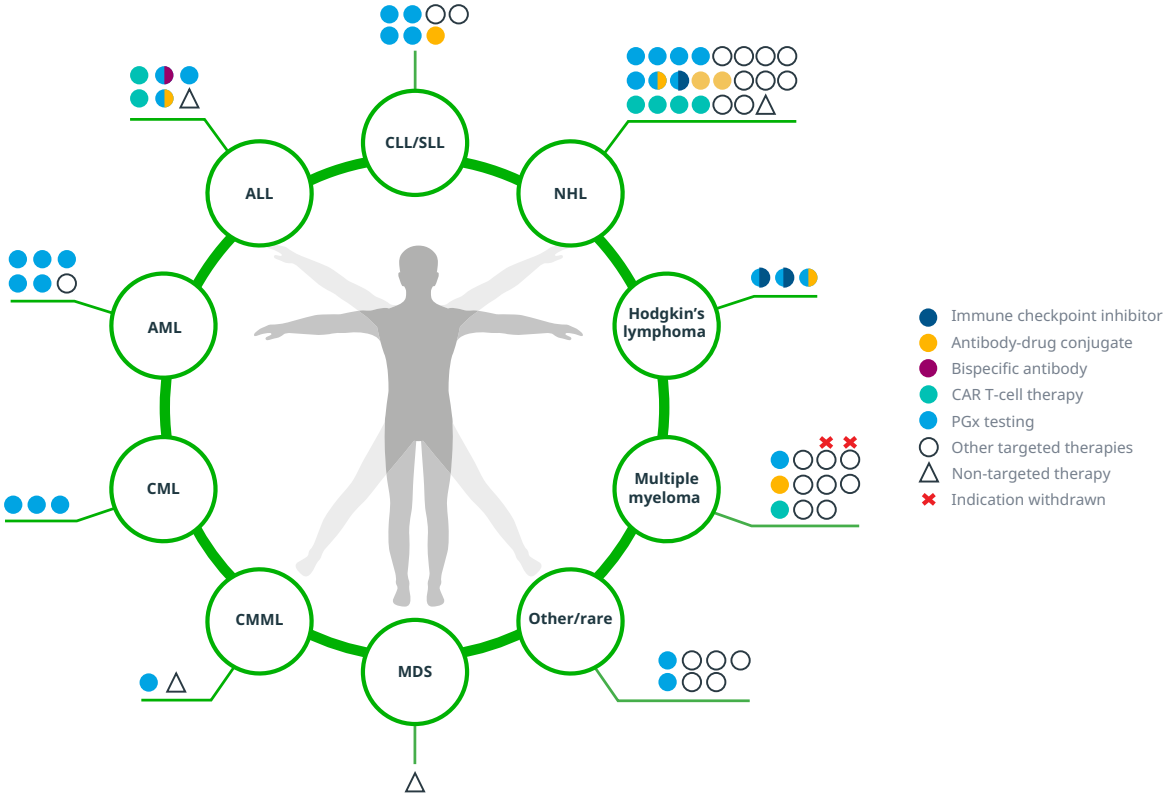
Source: IQVIA Institute, May 2022.

- Ninety-six novel cancer drugs have launched in the U.S. since 2011 to treat solid tumors, with 25 approved for multiple indications since launch.
- Significant innovation has occurred in lung cancer, with 30 products launched and predominantly targeted therapies for a variety of biomarker subtypes, including eight checkpoint inhibitors and one bispecific antibody.
- Breast cancer has had 17 new medicines launched for treatment since 2011, including three antibody-drug conjugates targeting HER2-positive and triple-negative breast cancer.
- Most novel cancer treatments utilize pharmacogenetic testing (PGx) providing personalized care to ensure the appropriate dose and drug are selected for each individual patient.
- Checkpoint inhibitors have provided significant therapeutic improvements across a range of solid tumors; however, nine indications have been withdrawn or revoked for these drugs following accelerated approval.[1]

Notes: Oncology excludes supportive care. Targeted therapies are cancer treatments that target specific genes and proteins that are involved in the growth and survival of cancer cells. PGx testing is a type of genetic test that assesses a patient's risk of an adverse response or likelihood to respond to a given drug, informing drug selection and dosing. Gynecologic cancers include cervical cancer, endometrial cancer, and ovarian cancer. Neurologic cancers include neuroblastoma and neurofibromatosis. Other gastrointestinal includes cholangiocarcinoma, gastroenteropancreatic neuroendocrine tumors, and pancreatic cancer. Other/rare includes cancers associated with von Hippel-Lindau disease, pleural mesothelioma, tenosynovial giant cell tumor, and neuroendocrine tumors. Skin includes basal cell carcinoma, melanoma, merkel cell carcinoma, and squamous cell carcinoma. Products with multiple attributes are represented with more than one color. Products may be approved for more than one indication within each type of cancer (e.g., small cell lung cancer and non-small cell lung cancer) but are only represented once; withdrawals are only indicated if the product had all approvals within that group of cancers withdrawn or revoked.

In the U.S., 55 unique new hematological cancer medicines have been launched since 2011

Exhibit 9: U.S. NASs in hematology-oncology launched 2011–2021 with indications including those granted after initial launch



Source: IQVIA Institute, May 2022.

- Fifty-five novel hematological cancer drugs have launched in the U.S. since 2011, with 17 approved for multiple indications since launch.
- Non-Hodgkin's lymphoma has seen the most innovation in hematological cancers, with 23 new drugs launched since 2011. This includes four CAR T cell therapies and three antibody-drug conjugates predominantly for the treatment of relapsed or refractory large B-cell lymphoma.
- Twelve new drugs have been launched since 2011 to treat multiple myeloma, including a CAR T cell therapy and antibody-drug conjugate. Another CAR T cell therapy was launched for multiple myeloma in early 2022 (not shown). Notably two products for the treatment of multiple myeloma have been withdrawn, with one of them just having launched in 2021.
- Although fewer novel drugs have been launched for leukemias, there have been important steps in innovation particularly for acute lymphoblastic leukemia, which has had two CAR T cell therapies, a bispecific antibody and an antibody-drug conjugate introduced for treatment in the last decade.

Notes: Oncology excludes supportive care. ALL=acute lymphoblastic leukemia; AML=acute myeloid leukemia; CLL=chronic lymphocytic leukemia; CML=chronic myeloid leukemia; CMML=chronic myelomonocytic leukemia; MDS=myelodysplastic syndrome; SLL=small lymphocytic lymphoma. Targeted therapies is a cancer treatment that uses drugs to target specific genes and proteins that are involved in the growth and survival of cancer cells. PGx testing is a type of genetic test that assesses a patient's risk of an adverse response or likelihood to respond to a given drug, informing drug selection and dosing. Other/rare includes advanced systemic mastocytosis, blastic plasmacytoid dendritic cell neoplasms, Castleman disease, Erdheim-Chester disease, myelofibrosis, and polycythemia vera. Products may be approved for more than one indication within each type of cancer (e.g., small cell lung cancer and non-small cell lung cancer) but are only represented once; withdrawals are only indicated if the product had all approvals within that group of cancers withdrawn or revoked.

New medicines launched in 2021 included significant clinical advances across a range of tumors and mechanisms

Exhibit 10: NASs launched in 2021 and summary of clinical benefits

INDICATION	MOLECULE	PROFILE
Acute lymphoblastic leukemia	asparaginase erwinia chrysanthemi	The determination of efficacy was based on a demonstration of the achievement and maintenance of nadir serum asparaginase activity (NSAA) above the level of 0.1 U/mL. An estimated 93.6% for patients maintained NSAA ≥ 0.1 U/mL at 48 hours after a dose of RYLAZE (JZP458-201)
Bone marrow suppression	trilaciclib	First therapy in its class to reduce the frequency of chemotherapy-induced bone marrow suppression in adults receiving certain types of chemotherapy for extensive-stage small cell lung cancer. Cosela may help protect bone marrow cells from damage caused by chemotherapy by inhibiting cyclin- dependent kinase 4/6, a type of enzyme
Cervical cancer	tisotumab vedotin	This review used the Assessment Aid. The objective response rate was 24% with a median response duration of 8.3 months (innovaTV 204)
Cholangiocarcinoma with FGFR2	infigratinib	FDA granted accelerated approval to infigratinib for metastatic cholangiocarcinoma. The ORR was 23% with 1 complete response and 24 partial responses. Median DOR was 5 months (CBGJ398X2204)
Chronic myelogenous leukemia	asciminib	FDA granted accelerated approval to asciminib. The main efficacy outcome measure was major molecular response. Major molecular response was achieved by 24 weeks in 42% of the patients. Major molecular response was achieved by 96 weeks in 49% of the patients
Endometrial cancer	dostarlimab	FDA granted accelerated approval of dostarlimab for dMMR recurrent or advanced solid tumors. The overall response rate was 41.6%, with 9.1% complete response rate and 32.5% partial response rate. Median DOR was 34.7 months (GARNET)
HER2 + Breast cancer	margetuximab	First HER2-targeted therapy to have improved progression-free survival (PFS) vs Herceptin. For metastatic HER2+ breast cancer, median PFS was 5.8 months vs 4.9 months in control arm (SOPHIA). For margetuximab arm, ORR was 22% with median DOR of 6.1 months compared to an ORR of 16% and median DOR of 6.0 months in the control arm
Large b-cell lymphoma	lisocabtagene maraleucel	First regenerative medicine therapy with RMAT designation to be licensed by the FDA. ORR was 73% with a complete response (CR) rate of 54%. The median DOR was one month. Patients who achieved CR, 65% had remission lasting at least 6 months and 62% had remission lasting at least 9 months. The estimated median DOR was not reached in patients who achieved a CR. The estimated median DOR among patients with partial response was 1.4 months (TRANSCEND)
Large b-cell lymphoma	loncastuximab tesirine	First CD19-targeted ADC approved as a single-agent treatment for adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL). The ORR was 48.3% with a complete response rate of 24.1%. After a median follow-up of 7.3 months, median response duration was 10.3 months (LOTIS-2)
Marginal zone lymphoma and follicular lymphoma	umbralisib	First-in-class dual PI3Kδ and CK1ε inhibitor. For marginal zone lymphoma, ORR was 49% with complete response rate of 16% and partial response rate of 33%. In follicular lymphoma, ORR was 43% with complete response rate of 3.4% and partial response rate of 39%. Median DOR was 11.1 months (UTX-TGR-205)

Exhibit 10: NASs launched in 2021 and summary of clinical benefits [CONTINUED]

INDICATION	MOLECULE	PROFILE
Multiple myeloma	melphalan flufenamide	First anticancer peptide-drug conjugate for patients with triple-class refractory Multiple Myeloma. ORR was 23.7% with 14.4% partial response rate and median DOR was 4.2 months (HORIZON)
Multiple myeloma	Idecabtagene vicleucel	First cell therapy approved for multiple myeloma. The ORR was 72% and complete response rate was 28%. An estimated 65% of patients who achieved CR remained in CR for at least 12 months
Neuroblastoma	naxitamab	FDA granted accelerated approval for pediatric patients one year of age and older and adults for neuroblastoma. A GD2-binding monoclonal antibody indicated for neuroblastoma. 45% ORR with 36% complete response and 9% partial response. Median DOR was 6.2 months
NSCLC with EGFR exon 20 insertion mutations	amivantamab	First treatment for adult patients with NSCLC who harbor EGFR exon 20 insertion mutations. The ORR was 40% with a median DOR of 11.1 months (CHRYSALIS)
NSCLC with EGFR exon 20 insertion mutations	mobocertinib	First-in-class, oral tyrosine kinase inhibitor. The ORR was 28% with a median response duration of 17.5 months
NSCLC with KRAS G12C mutations	sotorasib	This review used the Real-Time Oncology Review (RTOR) pilot program. The ORR was 36% with a median response duration of 10 months (CodeBreaK 100)
NSCLC with MET exon 14 skipping	tepotinib	First oral MET inhibitor. In naive patients, the ORR was 43% and median DOR is 10.8 months. In previously treated patients, the ORR was 43% with a median response duration of 11.1 months (VISION)
Prostate cancer	relugolix	The main efficacy outcome measure was medical castration rate, achieving and maintaining testosterone suppression as tumors are often hormone receptive. The medical castration rate was 96.7% in the relugolix arm (HERO)
Polycythemia vera	ropeginterferon alfa 2b	First FDA-approved medication for polycythemia vera, a rare hematological malignancy resulting in overproduction of red blood cells. The CHR in the treated population during the treatment period was 61%. The median DOR was 14.3 months (PEGINVERA)
Renal cell carcinoma	tivozanib	First therapy approved for adult patients with relapsed or refractory RCC following two or more prior systemic therapies. Median PFS was 5.6 months vs 3.9 months for those treated with sorafenib. Median OS was 16.4 and 19.2 months, for the tivozanib and sorafenib arms, respectively. The ORR was 18% for the tivozanib arm vs 8% for the sorafenib arm (TIVO-3)
Von hippel-lindau (VHL) disease with RCC hemangioblastomas, or pancreatic neuroendocrine tumors PNET	belzutifan	First HIF-2α inhibitor therapy approved in the U.S. An overall response rate of 49% was reported in patients with von Hippel-Lindau -associated renal cell carcinoma. The median duration of response was not reached. In patients with other von Hippel-Lindau-associated non-renal cell carcinoma tumors ORR of 83

Source: IQVIA Institute, Apr 2022.

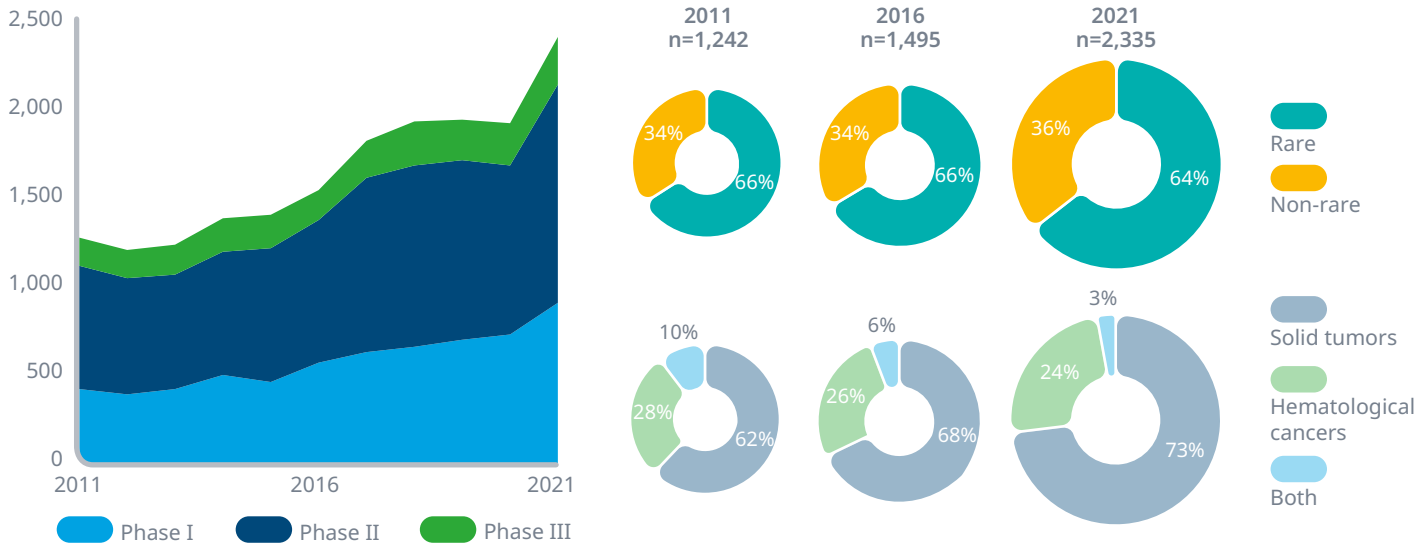
Notes: Summary of trials used as the basis for FDA approval of relevant drugs. ORR=overall response rate, CR=complete response, DOR=duration of response, PFS= progression-free survival, RMAT=Regenerative medicine advanced therapy designation.

Oncology research and development activities

- Oncology trial starts reached historically high levels in 2021, up 56% from 2016 and mostly focused on rare cancer indications.
- Cancer trials focus on metastatic or advanced cancers but trials for early cancer and vaccines have more than doubled in 10 years.
- Emerging biopharma companies were responsible for 68% of the oncology pipeline in 2021, up from 45% a decade ago.
- Composite success rates in oncology have been trending down since 2015 while rare oncology remains the highest.
- Oncology trials are substantially more complex than other disease areas but are often able to have fewer subjects.
- Number of subjects in oncology clinical trials is growing while accelerated approvals tend to be based on fewer subjects.
- Oncology trials have longer durations than other diseases but with increasing accelerated approvals, many do not conduct all phases.
- Oncology trials have significantly less “white space” than other therapy areas.
- Clinical development productivity indices for oncology extends a decade-long trend as lowest of all diseases.
- Approximately 80% of ongoing trials have molecular targets which would require pediatric trials under the RACE for Children Act.
- Oncology trials more frequently use novel trial designs than trials for other diseases.
- Development of next-generation biotherapeutics for hematological cancers has grown significantly since 2016.
- The next-generation biotherapeutic pipeline is focused on cell therapies, particularly CAR T in hematological cancers.
- >5.500 clinical trials investigate PD-1/L1 inhibitors, 80% of which are combinations, putting huge pressure on recruitment.
- Antibody drug conjugates are emerging with significant efficacy across a broad range of targets, while some targets have failed.
- Two bispecific antibodies are marketed globally for oncology with many in development for rare hematological cancers.

Oncology trial starts reached historically high levels in 2021, up 56% from 2016 and mostly focused on rare cancer indications

Exhibit 11: Oncology clinical trial starts by year, 2011–2021



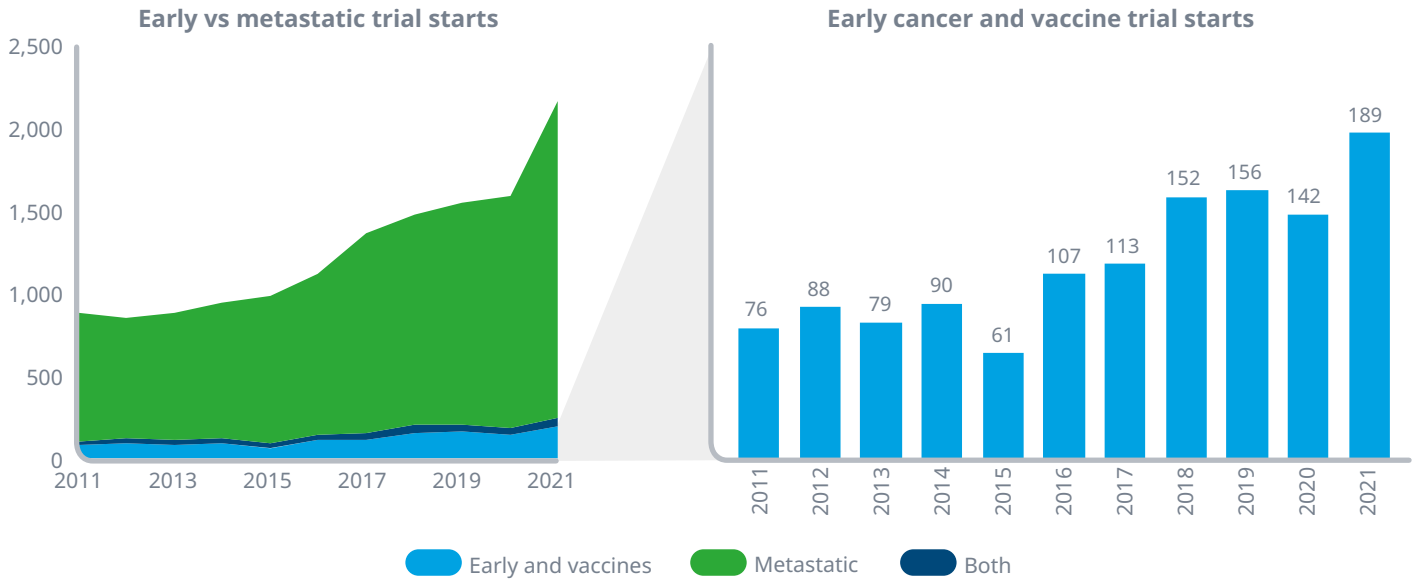
Source: Citeline Trialtrove, IQVIA Institute, Apr 2022.

- Oncology trials represent a significant portion of all clinical trials and reached historic levels in 2021, up 56% from the number of trials started in 2016 and with an increase of 25% from 2020 to 2021.
- Phase II trials, including Phase I/II, IIa and IIb, represent the majority of trials, with 51% of oncology trials started in 2021 being Phase II compared to 38% Phase I and 11% Phase III.
- Most oncology trials are focused on rare cancers, with two-thirds of trial starts over the last decade focused on bringing new treatments to these cancers with smaller patient populations.
- Oncology clinical trials are increasingly focused on solid tumors, with 73% of trials started in 2021 testing drugs against solid tumors only, up from 68% in 2016 and 62% in 2011.
- Although trials addressing hematological cancers represent a declining share of the total oncology trials, the number of trials rose 43% from 2016 to 2021, with more than 500 trials investigating drugs for treatment of hematological cancers only started in 2021.

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 involved with their initiation, partial execution and termination. Trials were industry sponsored, interventional trials and device trials were excluded.

Cancer trials focus on metastatic or advanced cancers but trials for early cancer and vaccines have more than doubled in 10 years

Exhibit 12: Oncology trial starts by the targeted stage of disease



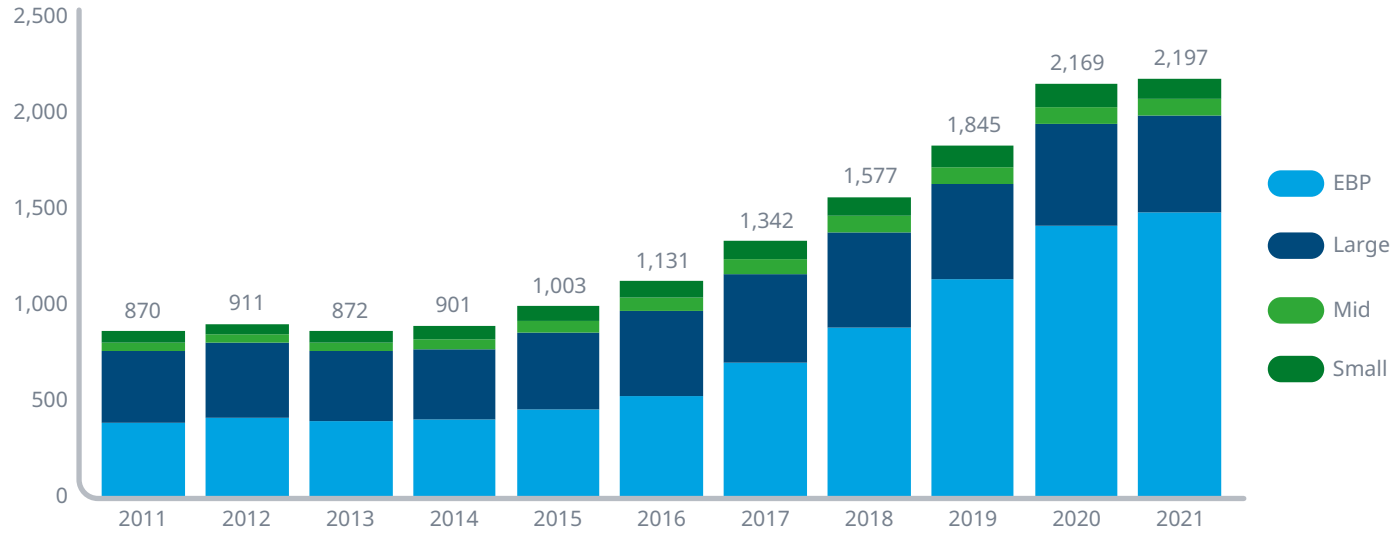
Source: Citeline Trialtrove, IQVIA Institute, Apr 2022.

- For decades, oncology clinical trials have tended to focus on metastatic/advanced tumors, prioritizing those patients most in need, and today those trials represent 89% of trial starts.
- Research focused on early cancers and vaccines has more than doubled in the last decade, with nearly 200 trial starts in 2021, representing 11% of oncology trial starts.
- This research has grown in line with overall cancer research, however, representing the same 11% of trials as a decade ago.
- Research focused on early cancers is challenging because patients are rarely diagnosed early enough to be enrolled in a dedicated trial for early disease.
- Most patients who might be a target for an early cancer trial respond well to existing treatments and may be less interested in enrolling in a clinical trial.

Notes: Trials were industry sponsored, interventional trials and device trials were excluded. Terminated trials were excluded. Early trials are those with patient segments: adjuvant and/or neoadjuvant treatment; Stage I and/or Stage II and/or Stage III; or Stage III only. Metastatic trials are those with patient segments: Stage IV; Line of Therapy; Maintenance/Consolidation Therapy; or haematologic cancers.

Emerging biopharma companies were responsible for 68% of the oncology pipeline in 2021, up from 45% a decade ago

Exhibit 13: Number of phase I to regulatory submission oncology pipeline products by company segment, 2011–2021



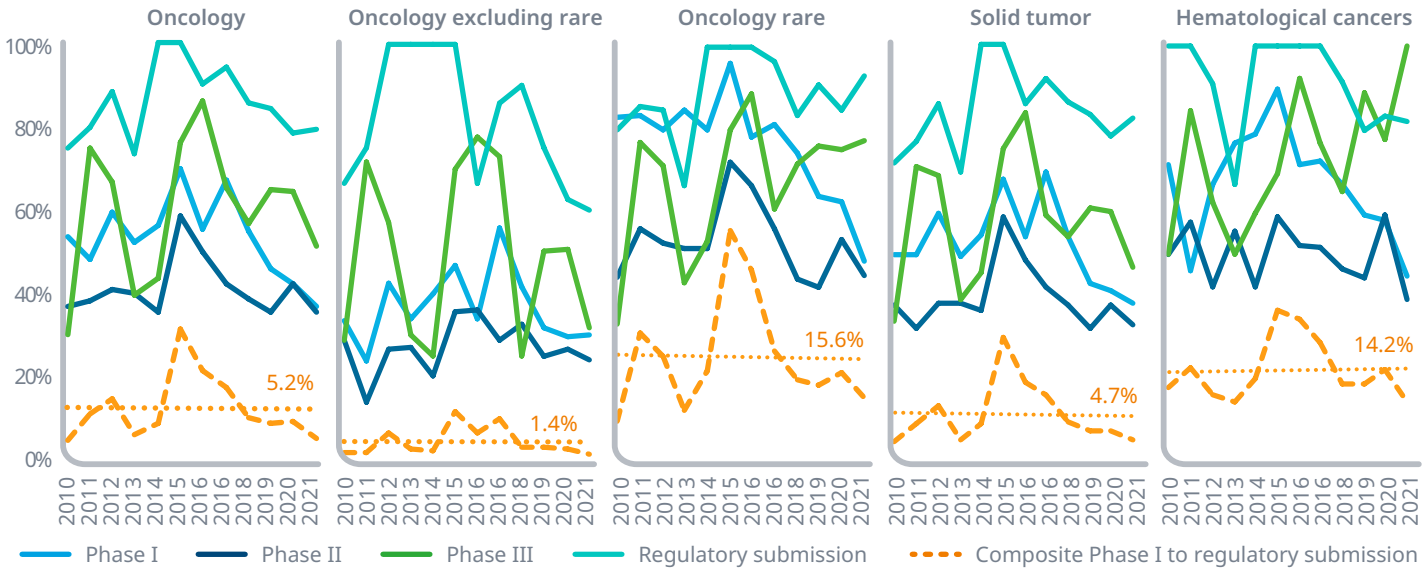
Source: IQVIA Pipeline Intelligence, Dec 2021; IQVIA Institute, Apr 2022.

- The number of products under development in oncology has grown significantly over the last decade, with more than 2,000 products currently under development.
- Emerging biopharma companies — defined as those with less than $500 million in annual sales and R&D spending less than $200 million per year — are responsible for 68% of products currently under development for cancers, an increase from 47% in 2016.
- Large pharma companies — those with greater than $10Bn in annual sales — have seen a declining share of the oncology pipeline, responsible for 23% of products currently under development, down from 39% in 2016.
- Of the emerging biopharma companies working in oncology, 78% are solely focused on oncology drug research and development and 72% are only developing a single drug.
- Increasing amounts of oncology research and development are occurring in China, which is now responsible for 19% of the oncology pipeline, highlighting the important role that companies headquartered there will play in the development of new products globally.

Notes: Analysis includes medicines in active research with a focus on cancer therapeutics and does not include supportive care. Company segment when two or more companies are involved is determined by the larger sales segment. Small companies have global sales between $500 million and $5Bn per year. Mid-sized companies have global sales between $5Bn and $10Bn per year.

Composite success rates in oncology have been trending down since 2015 while rare oncology remains the highest

Exhibit 14: R&D phase and composite success rates by therapy area, 2010–2021



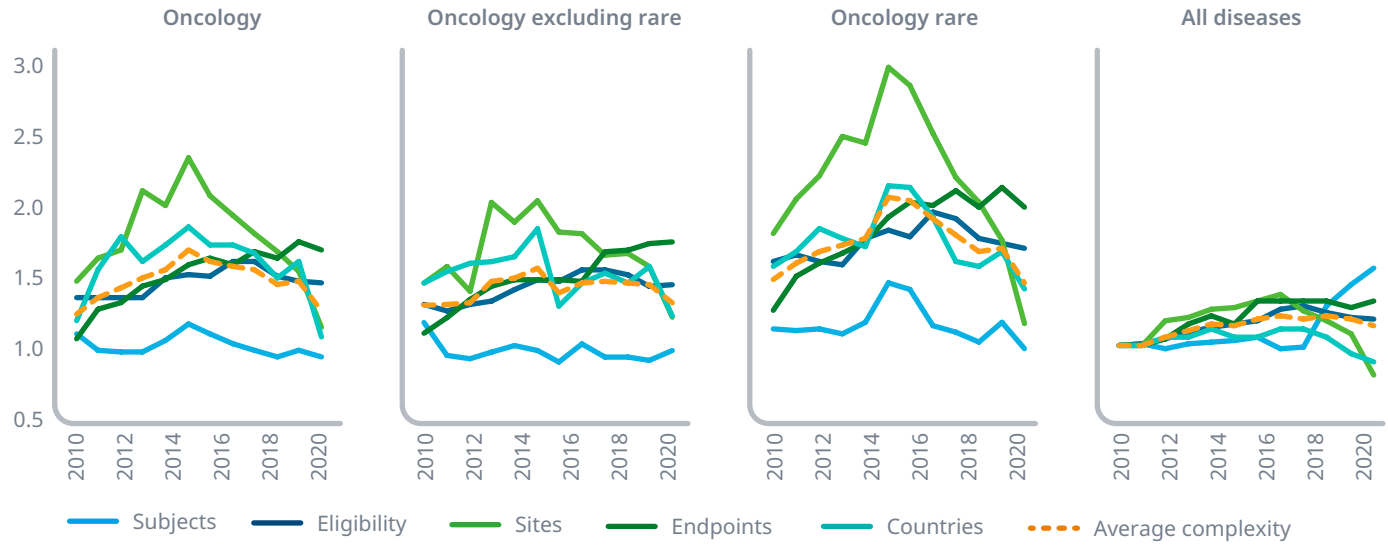
Source: IQVIA Pipeline Intelligence, Dec 2021; IQVIA Institute, Apr 2022.

- Oncology had one of the lowest composite success rates among all therapy areas in 2021, falling to 5.2%, which has been trending down since 2015.
- There is significant variability in success across oncology products, with those addressing rare and hematological cancers seeing higher success than those for non-rare cancers and solid tumors.
- Drugs being investigated for rare cancers saw an increase in success in 2021 in regulatory submission and Phase III, and a sharp decline in Phase I resulting in a composite success rate across all phases that fell from 22% in 2020 to 16% in 2021. This highlights a higher degree of rare cancer drugs reaching the market.
- Drugs under investigation for non-rare cancers face a higher degree of uncertainty, with only 1.4% success across all phases, which has remained relatively stable over the last 10 years.
- Drugs targeting hematological cancers tend to be more successful than those addressing solid tumors, with hematological cancer drugs three times more likely to reach the market than those for solid tumors.
- Composite success is based on success rates in each phase, which are based on progressing to subsequent research phases or regulatory approval anywhere in the world for any indication. In this way, a multi-indication cancer drug may be deemed a success when one indication is successful despite multiple indication failures.

Notes: Phase success rates are calculated as the percentage of products reaching a subsequent phase in the year out of the total 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. See methodology for more details.

Oncology trials are substantially more complex than other disease areas but are often able to have fewer subjects

Exhibit 15: Trial complexity by element and therapy area, 2010–2021



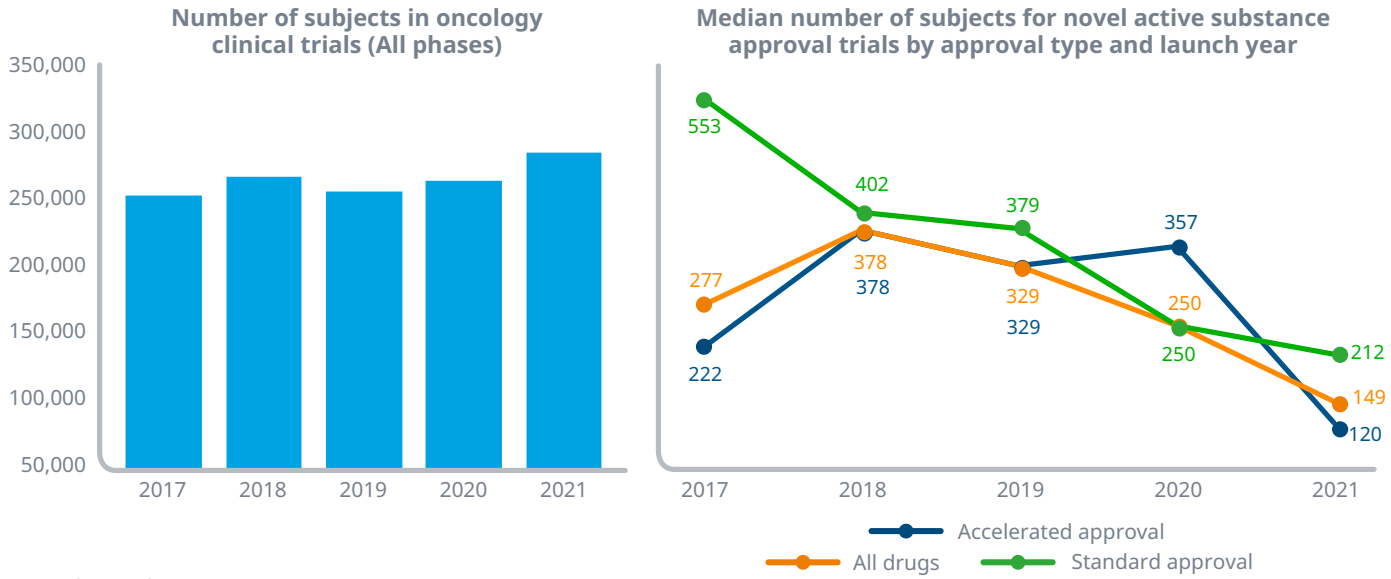
Source: Citeline Trialtrove, IQVIA Institute, Jan 2022.

- Oncology trials are among the most complex using the index, though this has been declining since 2015 and declined 14% in the last year compared to complexity across all diseases, which declined just 3%.
- Declines in oncology complexity can be attributed to significant drops in 2021 in the number of sites and countries as a result of the COVID-19 pandemic.
- Oncology trials overall have included an increasing number of endpoints since 2010, with rare oncology having the highest index indicating increasing evaluation of treatment outcomes.
- Rare oncology has seen declining complexity indices since 2015, mostly due to fewer sites, countries and subjects, signaling a focus on even smaller rare disease populations.
- 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.

Number of subjects in oncology clinical trials is growing while accelerated approvals tend to be based on fewer subjects

Exhibit 16: Oncology clinical trial subjects and number of subjects in novel active substance (NAS) approval trials by approval type



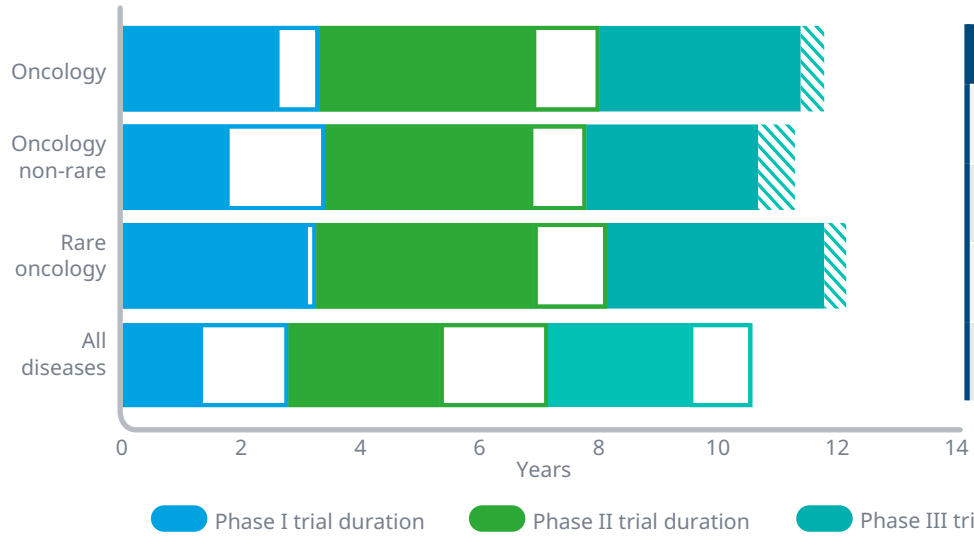
Source: Citeline Trialtrove, IQVIA Institute, Apr 2022.

- The number of patients enrolled in oncology clinical trials globally has grown by 40,000 in the last five years as the number of oncology clinical trials has grown.
- The number of subjects grew by 10% from 2020 to 2021 and 59% over the last decade, with oncology accounting for 13% of the industry's clinical trial subjects.
- Of the 83 NASs launched in the U.S. in the last five years, only 25% have had more than 500 patients in their approval trials.
- NASs receiving accelerated approval tend to have a lower median number of subjects, with the 14 NASs launched in 2021 with accelerated approval having 38 to 268 patients in their approval trials.
- The median number of subjects for NAS approval trials has been declining since 2017, particularly for those receiving standard approval. This downward trend reflects an increasing focus on smaller population cancers with large unmet needs and increasing regulatory latitude.

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

Oncology trials have significantly less “white space” than other therapy areas

Exhibit 17: Comparison of trial duration to phase-change duration (years), 2010–2021



TRIALS	WHITE SPACE	TOTAL DURATION
9.8	1.5	11.7
8.6	2.0	11.2
10.7	1.0	12.1
6.2	4.4	10.5

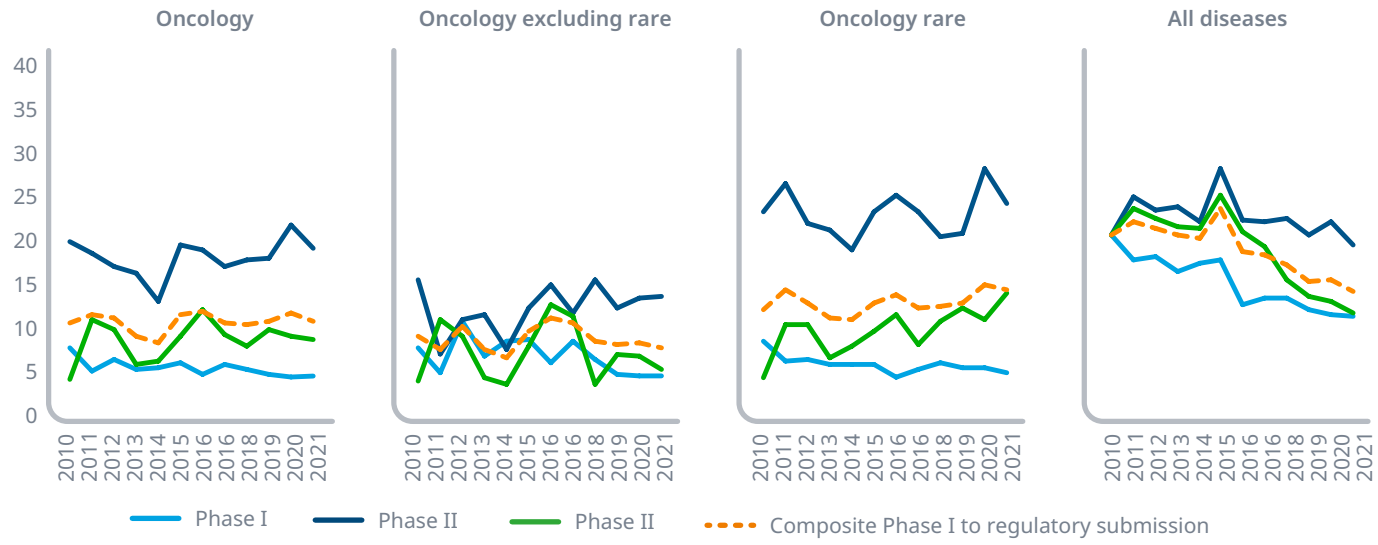
Source: IQVIA Pipeline Intelligence, Dec 2021; Citeline Trialtrove, IQVIA Institute, Jan 2022.

- Reducing “white space” — the difference between the time a molecule takes to progress through clinical development and its clinical trial duration — is a major area of focus for sponsors who still must balance clinical and commercial risk carefully.
- On average, new drugs spend 42% of their development time in white space on the way to the patient, with this dropping to 13% for oncology drugs.
- The proportion of white space is significantly different for rare and non-rare oncology drugs, with rare oncology drugs only spending, on average, 8% of total program duration in white space compared to 18% for non-rare oncology drugs.
- While oncology has the shortest average white space in the industry, it has the longest trial durations, and the trade-off of treatment and white space timing is likely partially driven by a high percentage of adaptive trials. Taking trial and white space time together, the total average program duration for oncology trials is nearly 12 years, almost one-and-a-half years longer than other disease trials.
- Oncology drugs are frequently submitted for regulatory review prior to final completion of their Phase III trials, allowing for earlier review of topline results in order to bring treatments to patients in an efficient manner.
- These results speak to a complex interplay between white space, trial timing and total program timing, with 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.” Oncology trials demonstrate substantial diversity in trial and phase duration and as a result, the average trial duration is longer than the average phase duration, illustrated with mixed chart series.

Clinical development productivity indices for oncology extends a decade-long trend as lowest of all diseases

Exhibit 18: Clinical development productivity across all phases by therapy area, 2010–2021



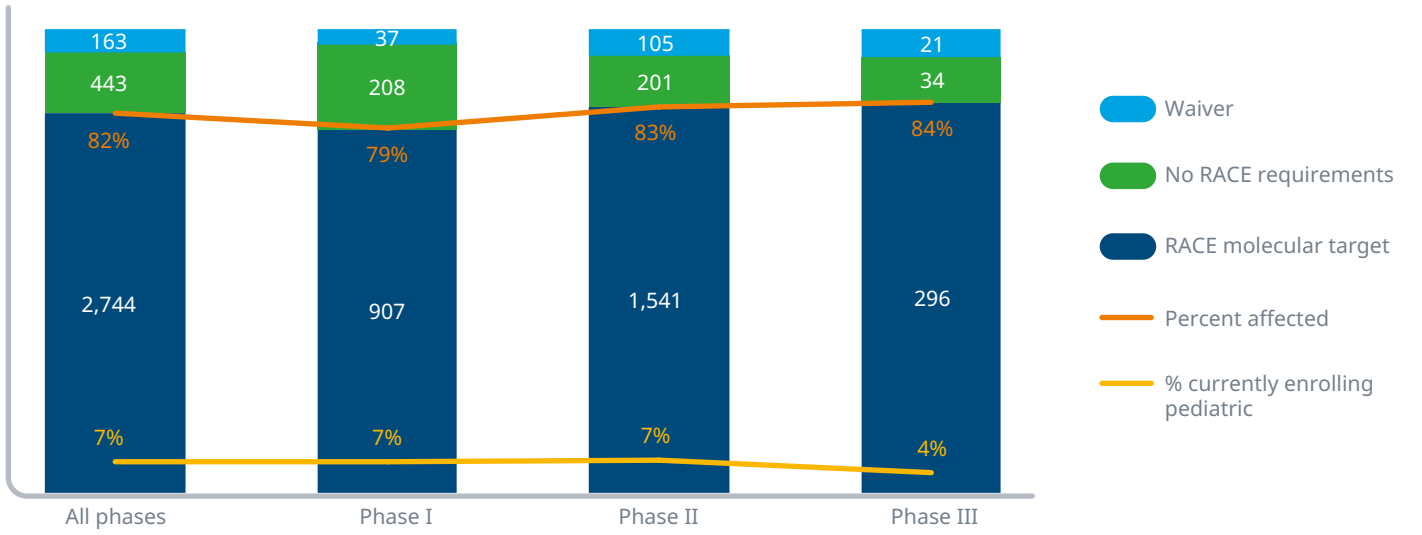
Source: IQVIA Pipeline Intelligence, Dec 2021; Citeline Trialtrove, IQVIA Institute, Jan 2022.

- Oncology clinical development productivity — defined as the complexity factored by duration, and then divided by the probability of success — has consistently been one of the lowest rates across the last decade.
- While productivity has declined across other disease areas, believed to be a result of increasing trial durations and decreasing probability of success, oncology productivity has remained relatively stable.
- Oncology productivity has been maintained due to a rise in productivity for rare oncology, driven by high productivity in Phase II and rising productivity in Phase III from decreased complexity and duration.
- Non-rare oncology productivity has declined since 2016 and is 15% below productivity seen in 2010, driven by low success, stable durations, and slight increases in complexity.
- While other diseases are seeing a productivity decline, rare oncology is rising steadily, especially in Phase II.

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.

82% of ongoing trials have molecular targets which would require pediatric trials under the RACE for Children Act

Exhibit 19: Number and percentage of clinical trials by RACE for Children Act impact



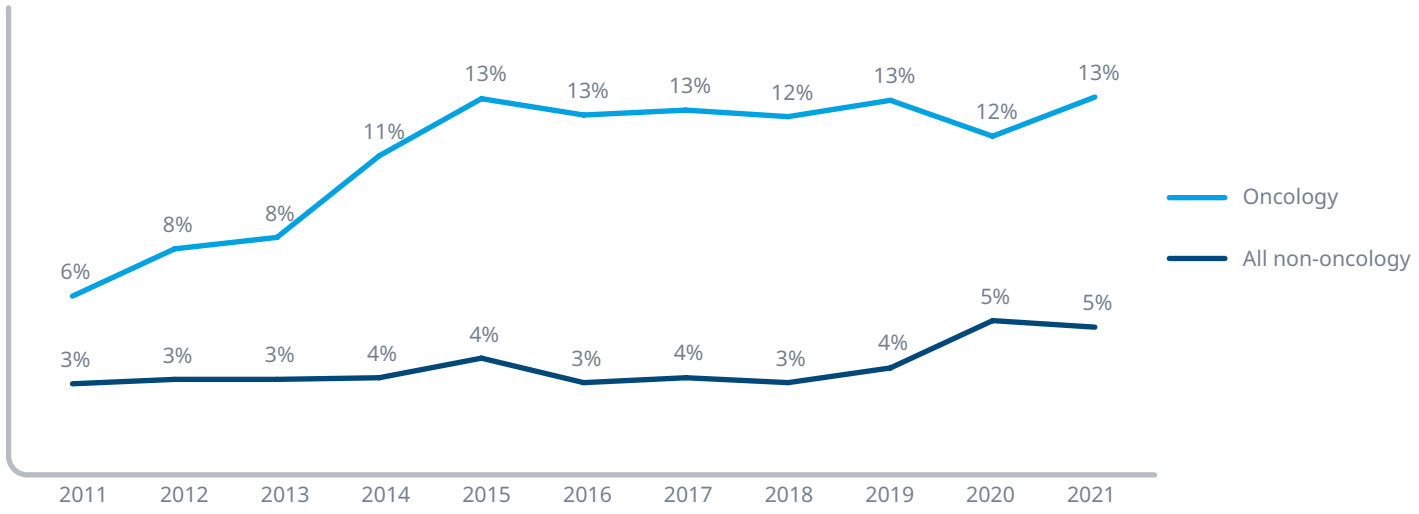
Source: Citeline Trialtrove, Apr 2022; IQVIA Institute, May 2022.

- The Research to Accelerate Cures and Equity (RACE) for Children Act passed in 2017 aimed to improve and expand treatment options for pediatric cancer patients by ensuring treatments under investigation for adult cancers are also tested in children when targeting molecular targets relevant to pediatric cancers.
- The legislation came as a response to significant innovation in targeted drug development for adult cancers that have rarely been investigated for pediatric cancers.
- The requirements apply to any new drug applications submitted to the FDA after August 2020 and require pediatric data for those directed at adult cancers and targeting biomarkers that research has shown play a role in pediatric cancers.[2]
- The legislation also eliminates previous exemptions for orphan drugs from similar pediatric requirements, which will be particularly impactful as more than 60% of cancer drugs in development are for rare cancers.
- A small set of molecular targets have evidence showing they are not associated with pediatric cancers, and new drugs targeting these are provided a waiver and do not require pediatric data upon submission.
- Of all ongoing oncology trials, 82% would be required to include children if they are investigating a novel active substance not yet submitted to FDA, and as of the end of 2021, only 7% of these trials include pediatric enrollees.

Notes: Trials are ongoing, industry sponsored, interventional trials. Marketed drugs were excluded to the extent possible. Trials investigating multiple drugs including a marketed drug remain.

Oncology trials more frequently use novel trial designs than trials for other diseases

Exhibit 20: Percent of trials with novel trial design by start date, 2011–2021



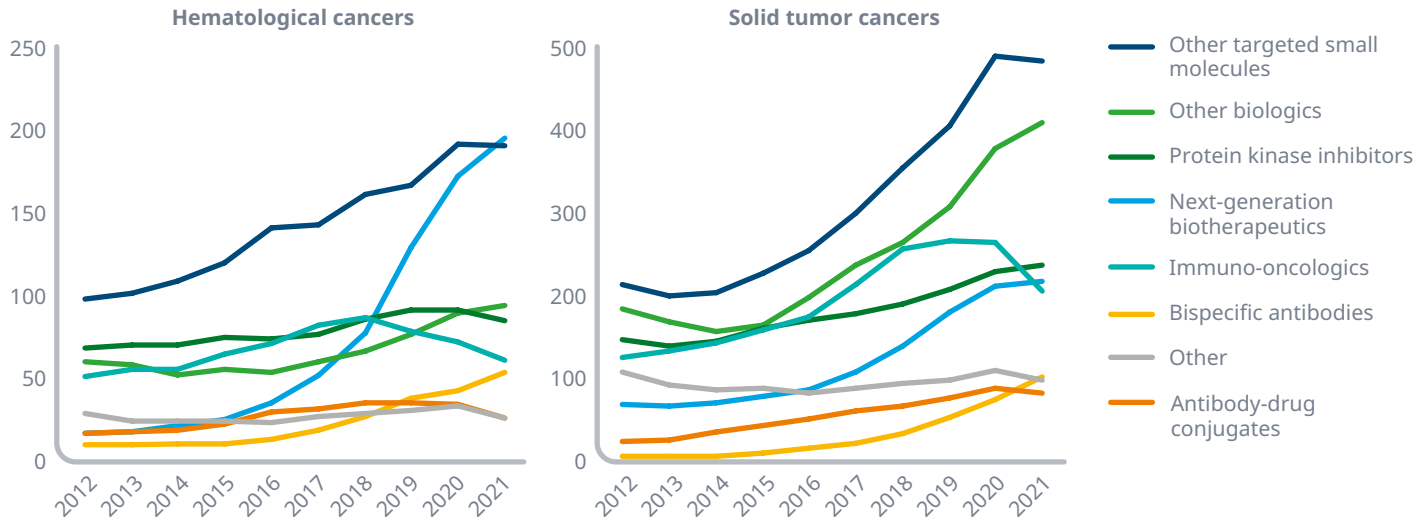
Source: Citeline Trialtrove, IQVIA Institute, Apr 2022.

- Novel trial designs in oncology — including adaptive, basket, umbrella, and master protocols — have nearly quadrupled in the last decade and were used in more than 550 trials started in 2021.
- Much of the growth in the use of novel trial designs in oncology occurred between 2011 and 2015, with the share of oncology trials utilizing novel trial designs remaining stable since 2015.
- Oncology trials more frequently utilize novel trial designs than trials for other disease areas, with 13% of oncology trials utilizing these mechanisms compared to just 5% in all other disease areas in 2021.
- Novel trial designs are predominantly utilized in Phase II trials for oncology (57%) which differs from all other disease areas where 50% of novel trial designs are utilized in Phase III trials. This is likely due to the fact that there are significantly fewer Phase III trials in oncology than other disease areas, as many oncology drugs receive approvals based on earlier phase trials.
- Oncology trials in general and novel trial designs, in particular, can have longer durations as patient recruitment becomes a growing challenge and contributes to growing numbers of drugs in Phase II slowly accruing patients.
- Novel trial designs are often more complex, but they can consolidate phases, provide program efficiencies, and identify responding patients more effectively across a range of options, potentially bringing treatments to patients on a shorter timeline.

Notes: Phase I, I/II, II, IIa, IIb, III and II/III trials only. Terminated trials are included to track the activity still involved with their initiation, partial execution and termination. Trials were industry and non-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.

Development of next-generation biotherapeutics for hematological cancers has grown significantly since 2016

Exhibit 21: Oncology R&D pipeline Phase I to regulatory submission by type, 2012–2021



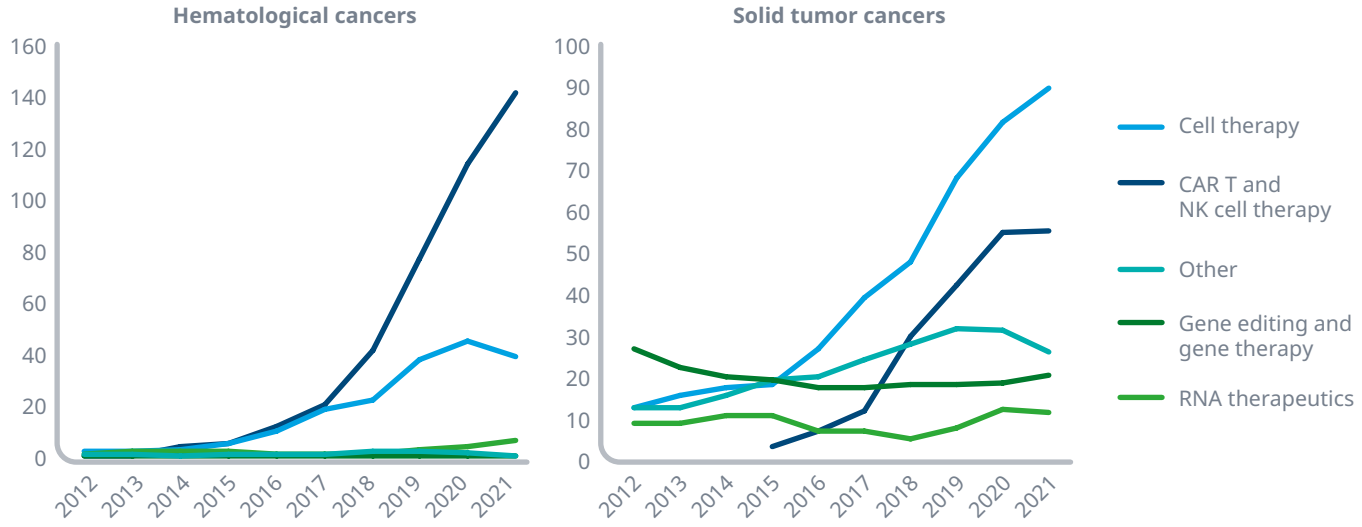
Source: IQVIA Pipeline Intelligence, Dec 2021; IQVIA Institute, Apr 2022.

- 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 there were only nine next-generation biotherapeutics under development for hematological cancers in 2012, this number has grown to 200 in 2021, 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 2020 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, with 49 under development for hematological cancers currently and 97 for solid tumors, 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.

The next-generation biotherapeutic pipeline is focused on cell therapies, particularly CAR T in hematological cancers

Exhibit 22: Oncology next-generation biotherapeutics Phase I to regulatory submission by mechanism, 2012–2021



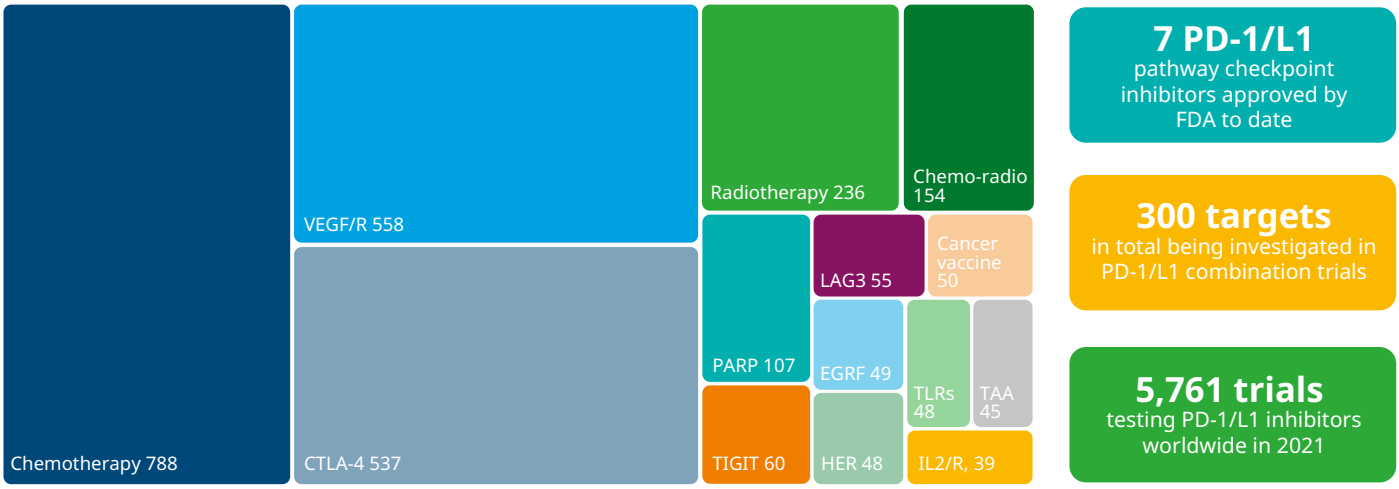
Source: IQVIA Pipeline Intelligence, Dec 2021; IQVIA Institute, Apr 2022.

- In 2021, 200 next-generation biotherapeutics were under development for hematological cancers, up from 9 a decade ago, and 212 for solid tumors, up from 63.
- Across all therapy areas, oncology accounts for 47% of the next-generation biotherapeutic pipeline, highlighting a significant amount of research and promise for using these products to improve care for cancer patients.
- Chimeric antigen receptor (CAR) T-cell and natural killer (NK) cell therapies represent 74% of the next-generation biotherapeutic pipeline for hematological cancers.
- Cell therapies, including CAR T cell and NK cell therapies, also have a significant amount of ongoing research for their use in treating solid tumors, with a number of cell therapies under development for prostate cancer, non-small cell lung cancer and liver cancer.
- Although gene therapies, including gene editing technologies such as CRISPR, used to make up a larger share of oncology next-generation biotherapeutics under development, research has slowed in recent years due to a significant number of adverse events in clinical trials. However, this has led to the implementation of proactive safety plans to ensure patient safety while investigating these products, which are still seen to offer significant promise.

Notes: Other includes RNA and DNA vaccines, oligonucleotides, and other less common next-generation biotherapeutics. Products being investigated for more than one type of cancer may be included in both hematological and solid tumor cancers.

>5,500 clinical trials investigate PD-1/L1 inhibitors, 80% of which are combinations, putting huge pressure on recruitment

Exhibit 23: Number of active trials per target for top 14 targets investigated in PD-1/L1 combination trials

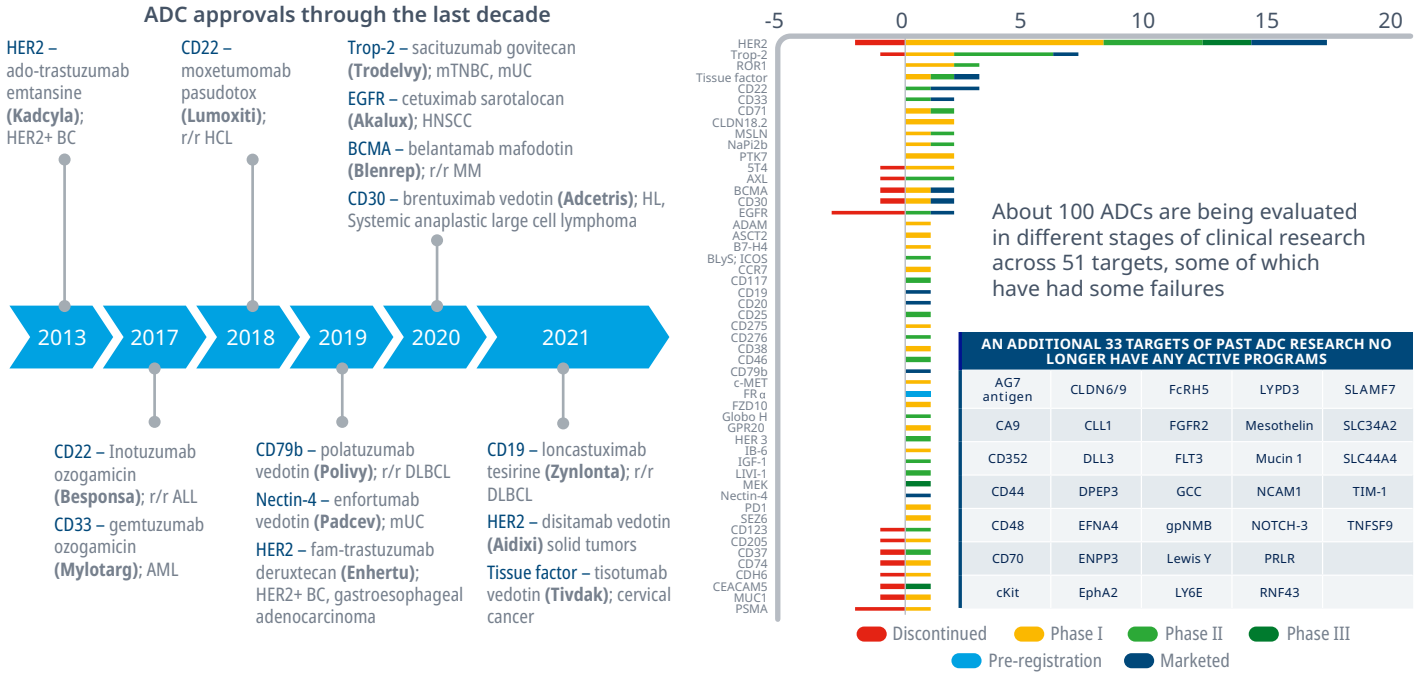


Source: Upadhaya S., Neftelinov S., Hodge J.,: Challenges and opportunities in the PD1/PDL1 inhibitor clinical trial landscape, Nature Reviews Drug Discovery, Feb 2022.

- The FDA approved the first PD-1/L1 checkpoint inhibitor, pembrolizumab (Keytruda), for patients with melanoma in 2014 and since then six additional PD-1/L1 inhibitors have been approved across a range of hematological cancers and solid tumors.
- There are currently 5,761 trials globally testing PD-1/L1 inhibitors, a 283% increase over the last five years.
- Nearly 90% of clinical trials with PD-1/L1 inhibitors starting in 2021 are investigating their use in combination with other drugs while monotherapy trials have been declining.
- These combination trials include drugs across 300 different targets and pathways, with PD-1/L1 in combination with chemotherapy accounting for 14% of all PD-1/L1 trials.
- CTLA-4 and VEGF/VEFGR are also important targets evaluated in combination therapies with PD-1/L1 inhibitors, accounting for more than 1,000 active trials in 2021. However, the investigation of PD-1/L1 inhibitors in combination with CTLA-4 inhibitors has been on the decline since 2017.[3]

Antibody-drug conjugates are emerging with significant efficacy across a broad range of targets, while some targets have failed

Exhibit 24: Antibody-drug conjugates approved and under development by target



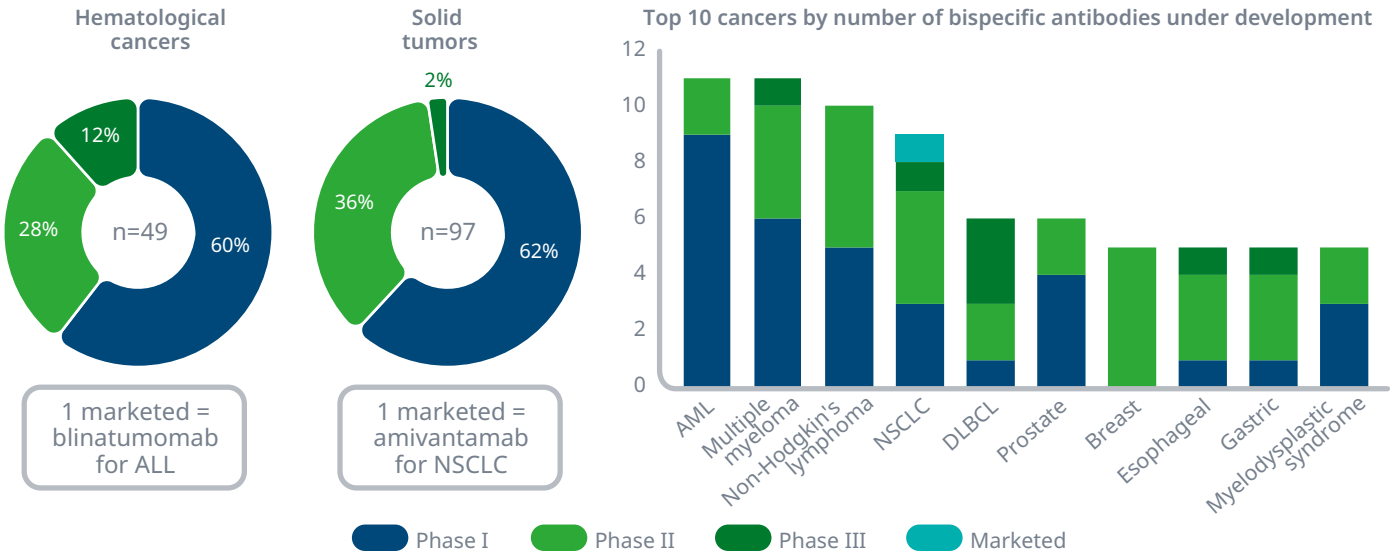
Source: IQVIA Pipeline Intelligence, IQVIA Institute, May 2022.

- Antibody-drug conjugates are becoming a more widely studied treatment option for cancers and consist of a monoclonal antibody linked to a cytotoxic agent, allowing for a targeted chemotherapy.
- The first antibody-drug conjugate approved for cancer, gemtuzumab ozogamicin (Mylotarg), received accelerated approval in 2000 but was later withdrawn from the market following serious safety concerns and then re-approved in 2017. Since 2000, 14 other antibody-drug conjugates have been approved across 11 different targets and predominantly for hematological cancers, although there have been significant solid tumor approvals particularly for breast cancer.
- Despite setbacks from discontinued research, there are 51 biomarker targets with ongoing antibody-drug conjugate research, with 17 products currently under development targeting HER2 and seven for Trop-2, common antigens expressed on a range of solid tumors.
- Thirty-three targets that were once thought to be promising targets for antibody-drug conjugates no longer have any active research, highlighting the difficulty of developing compounds that will provide significant benefits for cancer patients.
- Continued progress in antibody-drug conjugates in researching new targets, different cytotoxic agents, and enhanced molecular structures provide hope for patients that these compounds can provide significant improvements over traditional chemotherapy.[4]

Notes: CD20 directed Zevalin is not included in the timeline but was approved in 2002. Mylotarg initially received accelerated approval in 2000 but was later withdrawn and re-approved in 2017. ALL=acute lymphocytic leukemia; AML=acute myeloid leukemia; BC=breast cancer; BCMA=B-cell maturation antigen; DLBCL=diffuse large B-cell lymphoma; HCL=Hairy cell leukemia; HL=Hodgkin's lymphoma; HNSCC=head and neck squamous cell carcinomas; MM=multiple myeloma; mUC=metastatic urothelial cancer; r/r=relapsed refractory; TNBC=triple negative breast cancer.

Two bispecific antibodies are marketed globally for oncology with many in development for rare hematological cancers

Exhibit 25: Bispecific antibody pipeline by tumor and phase, 2021



Source: IQVIA Pipeline Intelligence, Dec 2021; IQVIA Institute, Apr 2022.

- Bispecific antibodies can bind multiple targets and act by bringing immune cells to cancer cells or through inhibition or activation of two separate targets.[5]
- There are currently only two bispecific antibodies on the market for treatment of cancer; blinatumomab (Blincyto) was marketed in 2014 for the treatment of acute lymphoblastic leukemia binding CD3 on T cells and CD19 on malignant B cells, while amivantamab (Rybrevant) was marketed in 2021 for the treatment of non-small cell lung cancer with EGFR exon 20 insertion mutations by binding and blocking EGFR and MET receptors on tumor cells.
- More than 130 bispecific antibodies are currently under development for cancer treatment, with more than 60% being investigated to treat solid tumor cancers, nearly 30% for hematological cancers, and nearly 10% being investigated for both.
- More than 60% of bispecific antibodies are in early clinical development, with only 12% of those under investigation for hematological cancers and 2% of those for solid tumors currently in Phase III trials.
- Bispecific antibodies are being tested across a range of cancers, with acute myeloid leukemia and multiple myeloma having significant development in hematological cancers and non-small cell lung cancer and prostate cancer with a number of drugs under development in solid tumors.

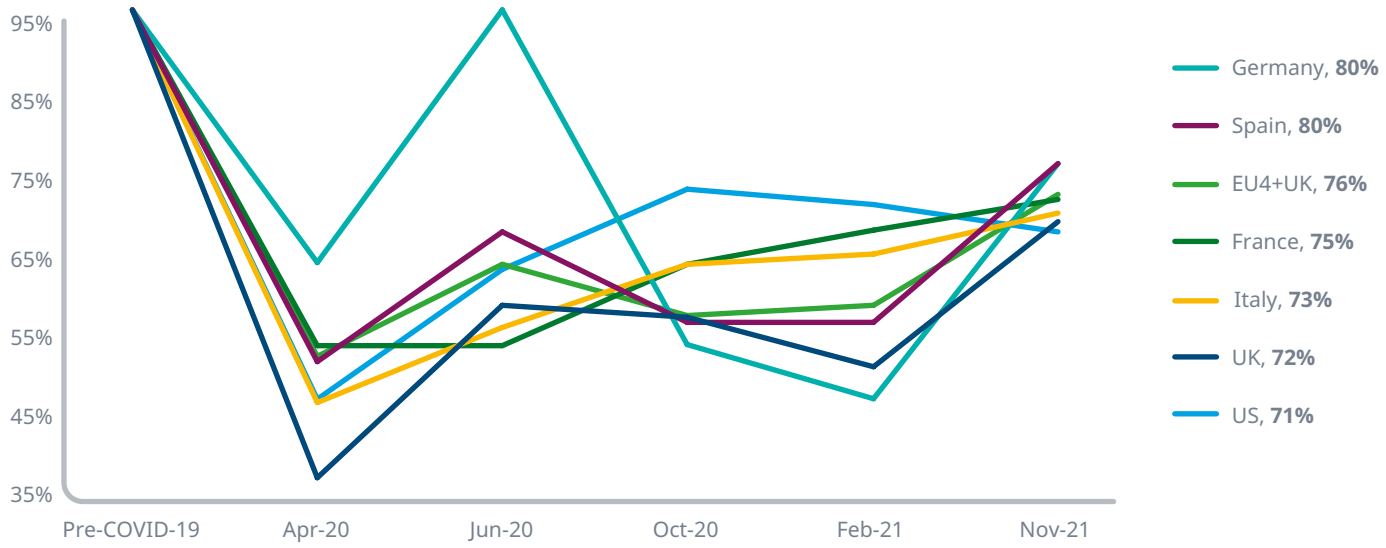
Notes: Analysis includes drugs in active research with a focus on cancer therapeutics and does not include supportive care. Products being investigated for more than one indication may be included in more than one disease area. Phase is determined by highest phase within each indication.

Impact of COVID-19 on cancer care

- Oncologists are reporting their caseload is still 20–29% below pre-COVID-19 levels.
- Delays in surgeries, chemotherapy and fewer diagnoses being conducted continue to be a concern for oncologists.
- Diagnostics used to screen and monitor cancer dropped dramatically and recovered, though deficits remain in pap smears.
- Over 30 million screenings for four common tumors disrupted, risking delayed or missed diagnoses for over 58,000 patients.
- More new patients presenting to community oncologists had metastatic disease in several tumors in the past two years.
- Since the start of the pandemic, oncologists in Spain and the UK have adopted remote consultations more than other countries, mitigating some disruptions to cancer care.

Oncologists are reporting their caseload is still 20-29% below pre-COVID-19 levels despite significant recovery in 2021

Exhibit 26: Percentage caseload vs pre-COVID-19 phase



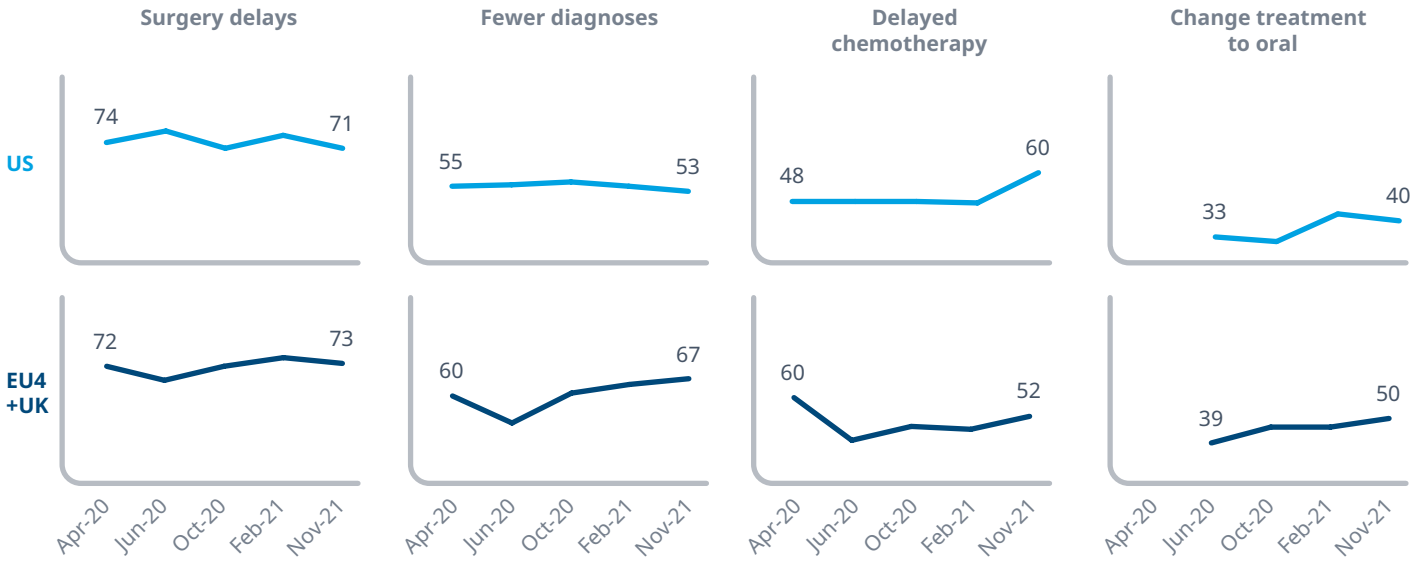
Source: IQVIA Impact of COVID-19 on the treatment of cancer reports – Nov 2021 – U.S. and EU4+UK.

- The COVID-19 pandemic has disrupted healthcare in substantial ways around the world, with the most concerning aspects related to patients with life-threatening cancers or coping with compromised immune systems associated with their treatment.
- The immediate effects of the pandemic were unprecedented as many countries declared lockdowns and introduced public health measures to contain transmission rates, including requirements in hospitals and medical practices.
- Soon after the start of the pandemic, oncologists across the U.S. and EU4+UK reported a 33-61% drop in their caseload.
- While caseloads improved in June 2020 and even returned to pre-COVID-19 levels in Germany, this has not been maintained, and as new waves of the pandemic have occurred, driven by variants of the virus, oncology patients remain below baseline.
- Although there has been improvement in patient caseload rates, as of November 2021, oncologists still report patient levels 20–29% below pre-COVID-19 levels.
- Reductions in caseloads could point to undiagnosed patients who may later present with more advanced cancer requiring more aggressive treatment and potentially poorer prognosis.

Notes: Data collection was in five waves with each wave including potentially different participants who were asked their pre-COVID-19 experience to enable comparison between waves.

Delays in surgeries, chemotherapy and fewer diagnoses being conducted continue to be a concern for oncologists

Exhibit 27: Oncologists survey responses regarding impacts to patient care due to COVID-19



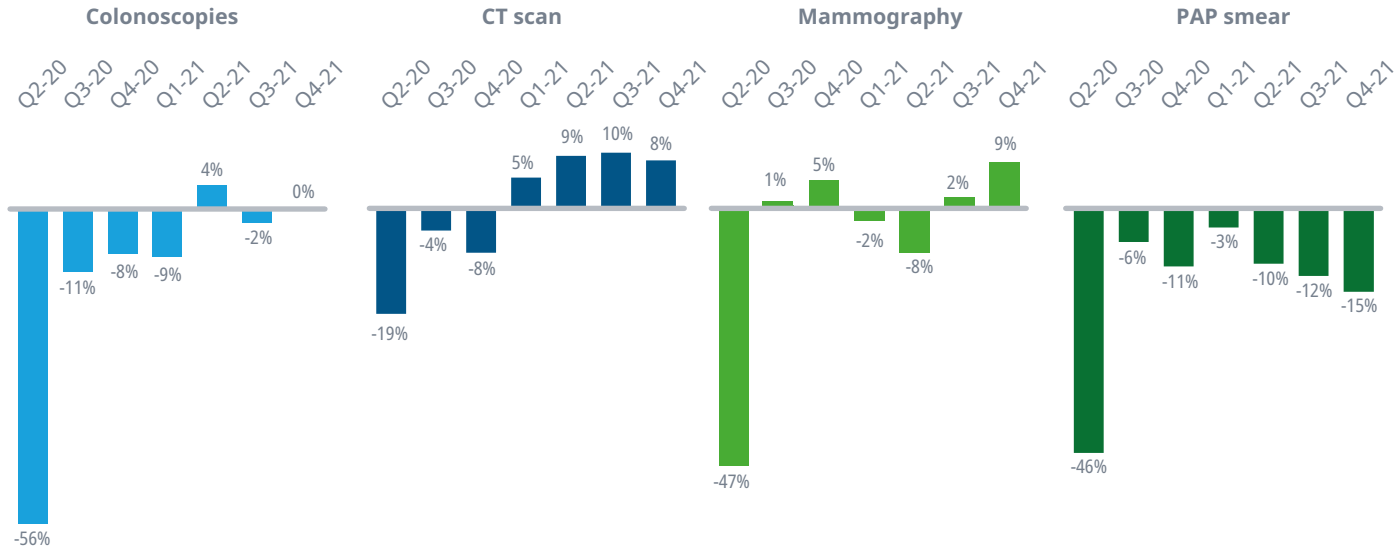
Source: IQVIA Impact of COVID-19 on the treatment of cancer reports – Nov 2021 – U.S. and EU4+UK.

- The immediate impact of COVID-19 was observed across cancer care, including surgery, diagnosis and treatment.
- Surgeries have seen the largest impact from COVID-19, with more than 70% of oncologists in the U.S. and EU4+UK continuing to report delays in surgeries in November 2021.
- Sixty-seven percent of oncologists in EU4+UK reported fewer diagnoses compared to 53% in the U.S. The consequence of delayed diagnosis will likely build as patients present with more advanced disease, known to lead to poorer outcomes.
- While 52% of oncologists in the EU4+UK continue to report delays in chemotherapy, an improvement from early in the pandemic, the U.S. saw an increase in November 2021, with 60% of oncologists reporting delays. Reducing risks from immunosuppression and continued waves of the pandemic have likely impacted treatment cycles.
- Oncologists across countries report varying impacts from COVID-19 on changing treatments to oral medications. On average, 50% of oncologists in EU4+UK in November 2021 reported changing to oral treatments, with this notably higher in the UK (73%). This is driven by guidelines from the NHS on interim treatment options to reduce hospital visits and allow for greater flexibility in cancer management.

Notes: Data collection was in five waves with each wave including potentially different participants who were asked their pre-COVID-19 experience to enable comparison between waves.

Diagnostics used to screen and monitor cancer dropped dramatically and recovered, though a 1–16% deficit remains

Exhibit 28: Reduction in diagnostic testing procedures at key time points compared to baseline expectations



Source: IQVIA Real World Claims, IQVIA Institute, Apr 2022.

- Screenings for common cancers are recommended for most adults with varying frequency based on age and risk factors.
- Significant disruption in cancer screenings occurred early in the pandemic with colonoscopies, mammograms and pap smears down more than 45% in Q2 2020.
- By the end of 2021, colorectal, breast and lung CT scans ranged from 0-9% above baseline levels while cervical cancer screenings recovered initially before steadily worsening relative to pre-pandemic levels.
- This continued reduction in screenings could lead to later detection and poorer prognosis for these patients.
- Low-dose CT scans for lung cancer screenings were less impacted by the pandemic, down 19% early on and recovering to higher levels from early in 2021. This is likely due to similarities in symptomology of lung cancer and respiratory viruses, and the resulting increased use of CT scans in evaluating lung function for COVID-19 patients.
- The early recovery in mammogram screenings is suggestive of increased public awareness around breast cancer screenings.
- Despite the significant disruptions to screenings in 2020, these diagnostics are unlikely to be conducted more frequently for these patients, and missed screenings suggest elevated risk for some patients for a missed cancer diagnosis or more severe cancer with a worse prognosis.

Notes: Quarterly claims compared to the average of weeks in the baseline period Jan 3, 2020 to Feb 28, 2020.

Over 30 million screenings for four common tumors disrupted, risking delayed or missed diagnoses for over 58,000 patients

Exhibit 29: Modeled cumulative impact of reduced screening tests through Q4 2021

	Colorectal	Lung	Breast	Cervical
# annually	10Mn	700K	42Mn	79Mn
% fewer due to COVID-19	-13%	-1%	-8%	-16%
# fewer tests Q2 2020 through Q4 2021	2.3Mn colonoscopies	12,250 CT scans	5.9Mn mammograms	22.1Mn pap tests
Rate of positive cancer diagnosis per test	1:91	1:112	1:200	1:5,274
Delayed cancer diagnosis due to COVID-19	25,000 patients	109 patients	29,400 patients	4,200 patients

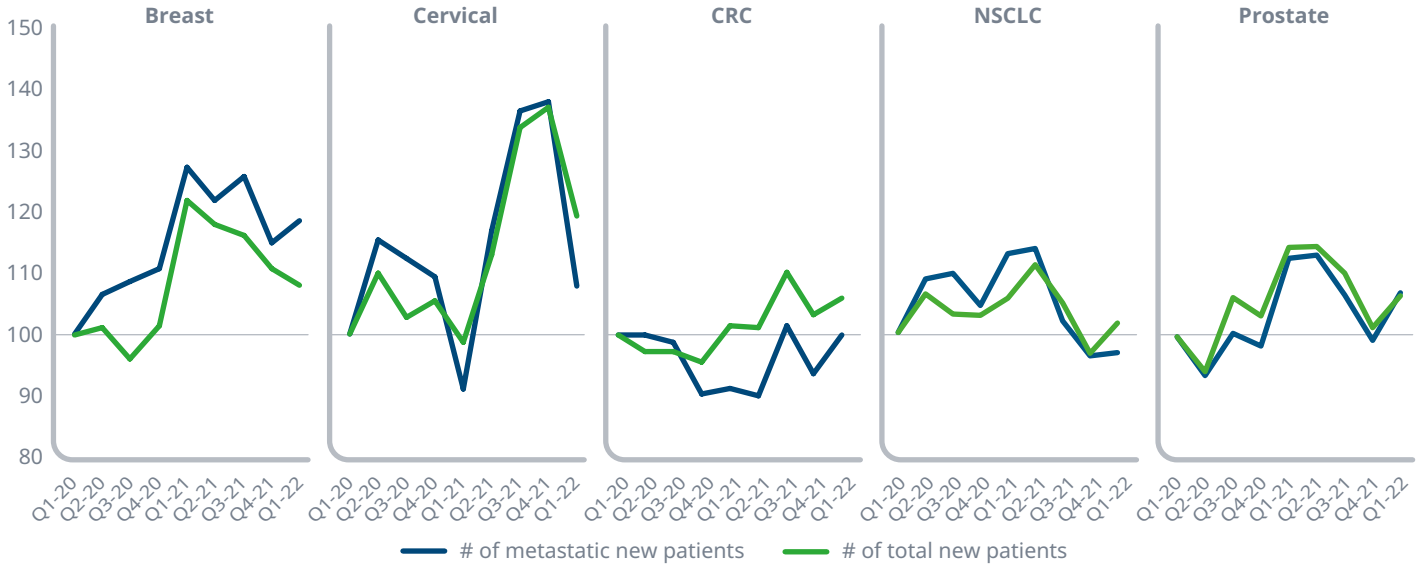
Source: IQVIA Real World Claims, American Cancer Society, IQVIA Institute, Apr 2022.

- More than 30 million screening tests were missed cumulatively from Q2 2020 through the end of 2021, based on the estimated annual screening tests in the U.S. for each cancer and the percentage reduction observed in medical claims.
- Literature shows that the rate of positive cancer diagnosis from these screening tests varies across cancer from 1 in 91 for colorectal cancer to 1 in 5,274 for cervical cancer, meaning varying numbers of potentially delayed diagnoses.
- For breast cancer, 5.9 million mammograms have been delayed through 2021, resulting in 29,400 patients that have not been diagnosed, which could lead to potentially more advanced disease and worsening prognosis as diagnosis continues to be delayed.
- Colonoscopies are down 13% with 2.3 million delayed through 2021, meaning potentially 25,000 patients with undiagnosed colorectal cancer.
- Despite 22.1 million delayed pap smears, the estimated number of patients with missed diagnoses of cervical cancer is 4,200 due to the low positivity rate. Delayed diagnosis is significant for this small group of patients who could require more complex treatment when eventually diagnosed.

Notes: Estimates of diagnostics were modeled from relevant tumor epidemiology sources. Positive diagnosis rates are from the American Cancer Society. Reduced numbers of claims are from IQVIA Real World Claims data, based on national claims data up to week ending Dec 31, 2021.

More new patients presented to community oncologists since the pandemic started and some tumors had more metastatic disease

Exhibit 30: U.S. total new patients, new metastatic patients compared to Q1 2020

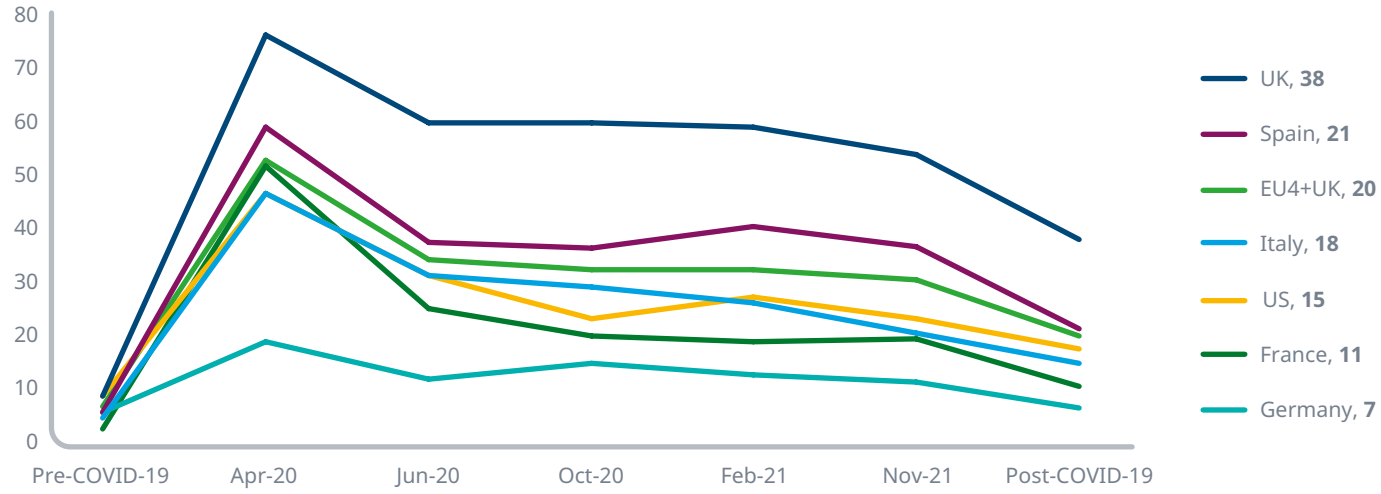


Source: IQVIA BrandImpact, Apr 2022.

- Oncologists have seen a larger number of new patients across five common cancers compared to pre-pandemic levels, ranging from a 1% increase in non-small cell lung cancer to a 20% increase in cervical cancer.
- New colorectal cancer patient numbers in the U.S. remained below pre-pandemic levels throughout 2020 with slight increases throughout 2021.
- Of significant concern is the increase in patients presenting with metastatic disease across the pandemic in all but colorectal cancer, likely driven by the reduced number of screenings for these cancers throughout the pandemic.
- Colorectal cancer patients have had the least disruption to overall patient numbers of any of the tumors and that has resulted in the negligible increase in the numbers of new patients presenting with metastatic disease.
- Cervical cancer has seen the largest increase of new patients and patients presenting with metastatic disease, with new patients with metastatic disease up 18% from pre-pandemic levels at the beginning of 2022 but peaking at 38% above pre-pandemic levels at the end of 2021.

Since the start of pandemic, oncologists in Spain and the UK have adopted remote consultations more than other countries

Exhibit 31: Percentage of patients on remote consultations – individual country breakdown



Source: IQVIA Impact of COVID-19 on the treatment ofcancer reports – Nov 2021 – U.S. and EU4+UK.

- The location of interactions between oncologists and cancer patients was also impacted as a result of the COVID-19 pandemic.
- There was a rapid shift to remote interactions reported in April 2020, which enabled continued management of cancer patients while countries experienced lockdowns.
- While remote interactions remained relatively high through 2020 and early 2021, there was a slight decline across countries toward the end of 2021; however, 53% of patients continued to be seen remotely in the UK in November 2021.
- Germany has seen relatively low use of remote consultations, with the proportion of oncology patients being managed remotely peaking at 19% early in the pandemic and declining to 12% by the end of 2021.
- Oncologists expect remote consultations will continue to play a role in cancer management to varying degrees across countries when the COVID-19 pandemic transitions to an endemic virus.
- In EU4+UK, oncologists expect 20% of consults will be remote, up from 7% pre-COVID-19, and notably in the UK where they expect 38% to be remote post-COVID-19, consistent with the systemic commitment to remote and virtual health system tools.
- Oncologists in the U.S. expect 15% post COVID-19 remote engagement, up from 5% before the pandemic.

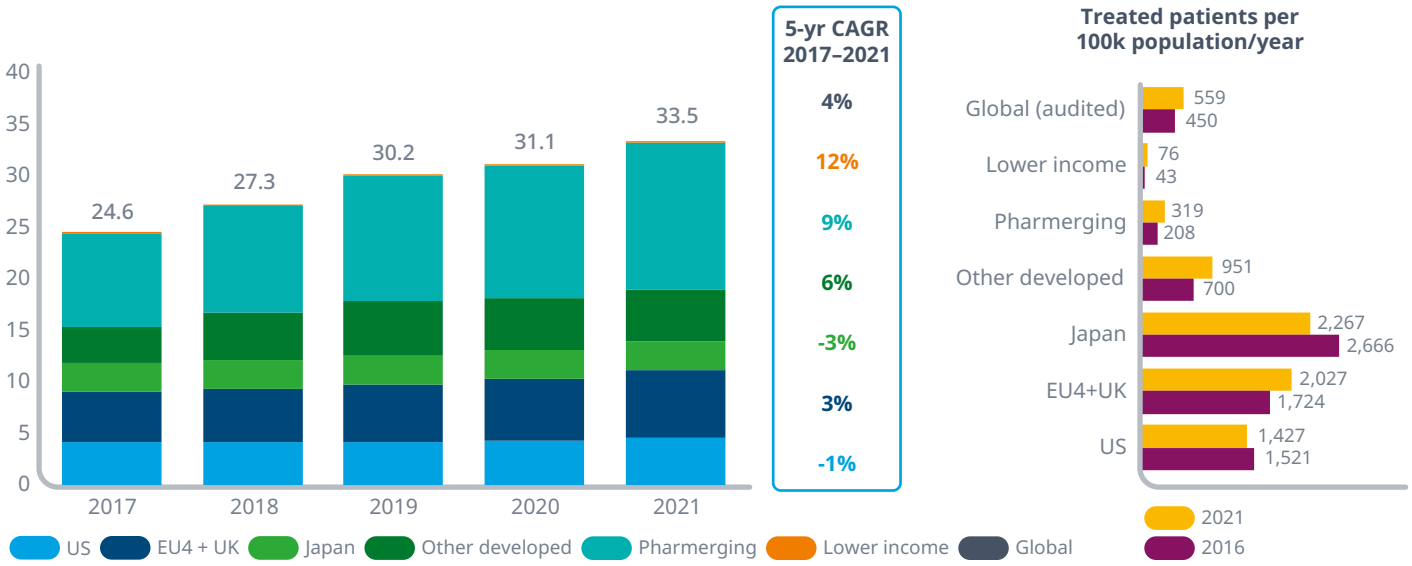
Notes: Data collection was in five waves with each wave including potentially different participants who were asked their pre-COVID-19 experience to enable comparison between waves.

Cancer patient access and use of scientific advances

- Global numbers of treated patients have increased at an average 4% over the past five years, and are expected to accelerate in next five years.
- Growth in the use of oncology medicines fell early in the pandemic but has returned to 2019 levels except in the EU4+UK.
- Country-specific differences exist in molecular testing across different tumor types and biomarkers, which drive the use of many novel therapies.
- Use of checkpoint inhibitors has risen rapidly in major markets with variations on a per capita basis and some lagging.
- Non-small cell lung cancer treatment has shifted to include checkpoint inhibitors as the standard of care in the past three years.
- Significant advances, primarily in immunotherapy, have extended median duration of first-line therapy with more responding.
- Melanoma is treated with immuno-oncology checkpoint inhibitors 80% of the time with rising use of combo regimens.
- Immunotherapies and PARP inhibitors have shifted treatment patterns in cancers affecting women especially in the last two years.
- There are 526 hospitals accredited with international standards for the administration of CAR T therapies globally.
- While the number of CAR T cell centers is growing, not all centers have all approved products available.

Global numbers of treated patients have increased at an average 4% over the past 5 years, to accelerate in next 5 years

Exhibit 32: Global oncology patient treatment regimens (millions), 2017–2021



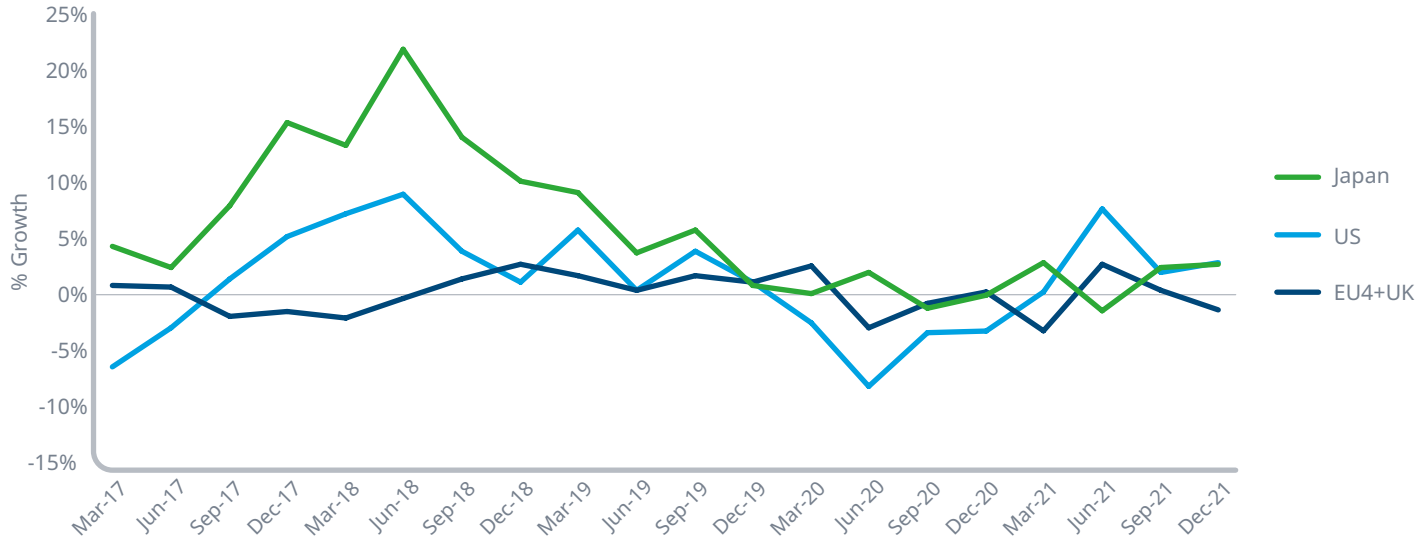
Source: IQVIA Oncology Link, World Bank Population Estimates, Dec 2021.

- Aging populations and robust access to care are driving steady levels of cancer treatment in developed markets.
- Widening access to care in lower income markets along with longer treatment durations are resulting in higher numbers of patients receiving treatment each year.
- Per capita rates of treatment remain highest in developed countries, averaging 5–10 times above the level in lower income and pharmerging countries.
- Most countries experienced some slowing of the growth of treated patients during 2020, related to disruptions from COVID-19, with a rebound in 2021 as health systems were able to return to historic levels of care and engagement.
- Over the past five years, the overall number of patient treatment regimens declined in the U.S. and Japan while rising in EU4+UK and other developed countries.

Notes: Patient treatment regimens reflect a specific combination of drugs used for a patient and counts each regimen and cycle received based on the estimation methods in Oncology Link. Pharmerging countries are defined as those with lower than $30,000 per capita income and 5-year forecast growth of the total pharmaceutical market of >$1Bn. Other developed countries are those countries with incomes above $30,000 which are not otherwise named. Lower income are a limited group of audited countries with lower incomes and not meeting the pharmerging 5-year growth criteria. Pharmerging and lower income countries often do not have audits covering all channels and may understate oncology usage and spending.

Growth in the use of oncology medicines fell early in the pandemic and has been partly offset since then, except in the EU4+UK

Exhibit 33: Growth in oncology volume in defined daily doses (DDD), 2017–2021



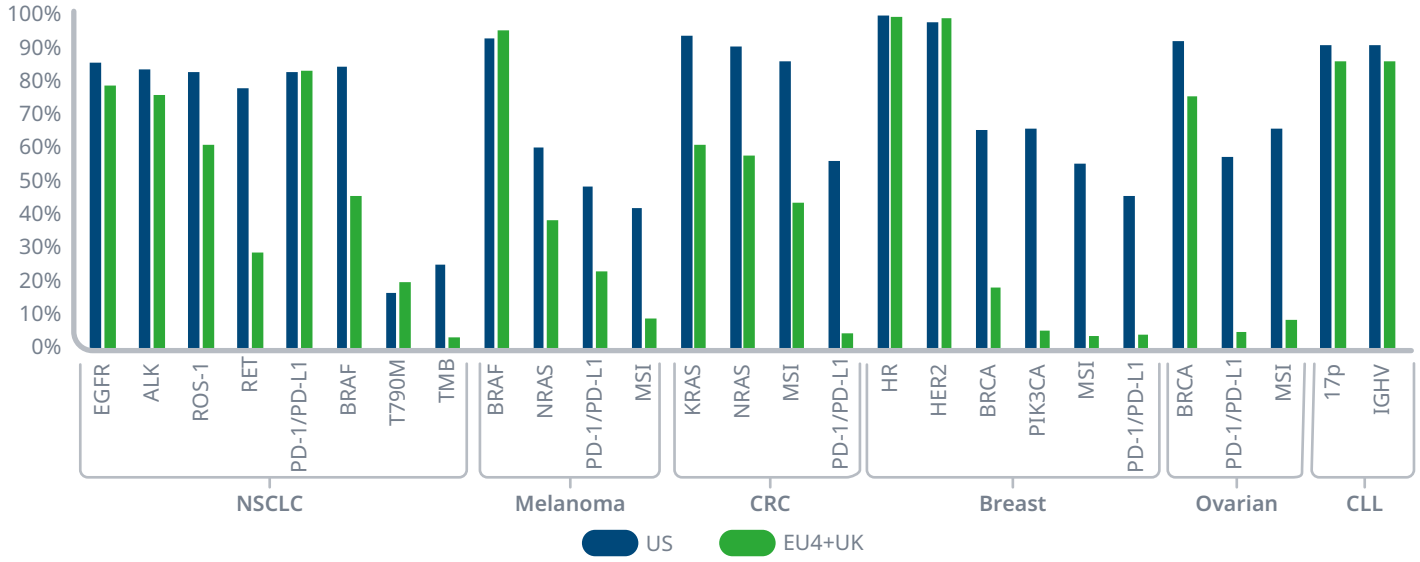
Source: IQVIA MIDAS, Dec 2021; IQVIA Institute, Apr 2022.

- Measuring each oncology therapeutic with a standardized daily dose, overall trends in usage have flattened during the pandemic, but do not reflect the same declines seen with other metrics such as oncologists' self-reported caseloads (see exhibit 26).
- The relatively stable growth trends are suggestive of a remarkably resilient system and patients continuing to receive ongoing cancer care despite the pandemic, though new patients may still be undertreated.
- In the U.S., defined daily doses declined 4.6% in 2020, and rebounded 3.1% in 2021, partly offsetting the disruptions in 2020, which were worst in Q2 as the pandemic's first wave hit.
- In the EU4+UK, overall days of therapy declined 0.4% in 2020 and a further 0.5% in 2021.
- In Japan, growth slowed to 0.1% in 2020, down from 4.7% in 2019, but rebounded to increase 1.5% over the pandemic low point.
- Standardized dosing analysis is helpful to determine general volume trends; however, it could mask shifts in real-world dosing, with some patients treated more intensively while others are absent due to COVID-19 disruptions to care.

Notes: Defined daily doses are based on the lead indication for each cancer drug and reflect the volume of medicine per day in the standard cycle. These assumptions are consistent with the approach to defined daily doses embedded in the World Health Organization Defined Daily Dose metric (WHO-DDD) while specific dosing assumptions have been researched and applied by the IQVIA Institute. Defined daily dose assumptions do not reflect real world dosing variations across patients, across tumors, or off-label use of medicines for other purposes. It is understood that some cancer medicines including bevacizumab may have had some off-label use for severe COVID-19 patients prior to the approval of specific COVID therapeutics, and as such inflate the estimated cancer days of therapy shown.

Country-specific differences exist in molecular testing across different tumor types and biomarkers

Exhibit 34: 2021 Testing rates by tumor, biomarker and geography



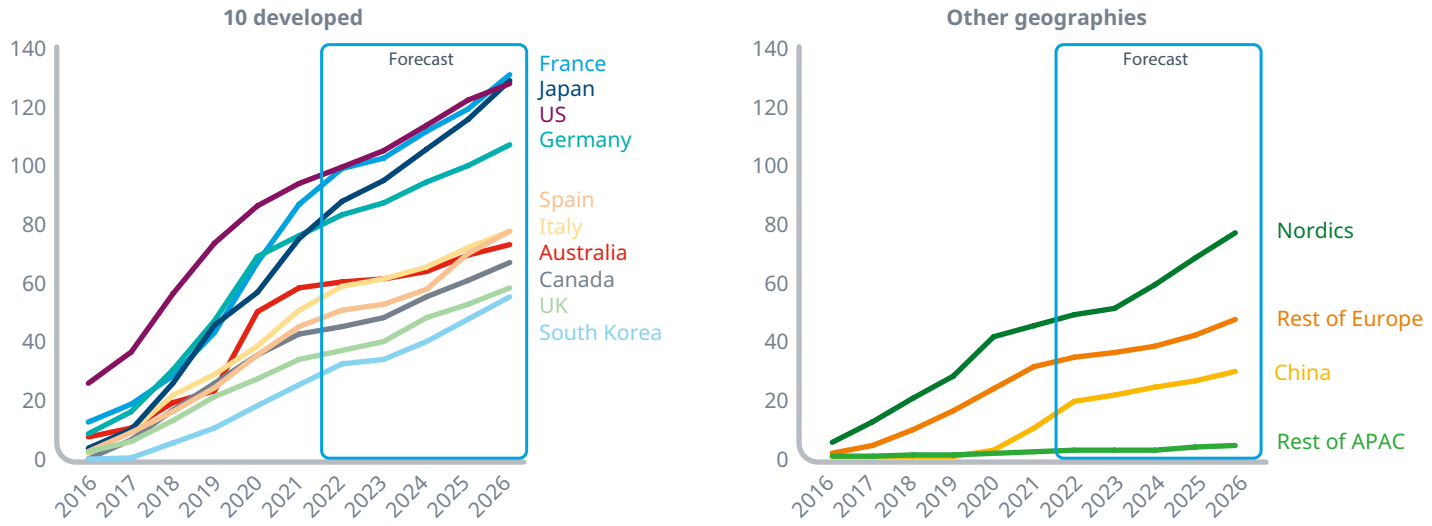
Source: IQVIA Oncology Dynamics, Dec 2021.

- Large geographic variations in testing rates suggest that patients may not yet have the fullest access to diagnostics and the novel medicines a positive test would support for treatment.
- Guidelines recommend testing NSCLC patients for EGFR and ALK biomarkers. More than 75% of patients are being tested in both the U.S. and EU4+UK, consistent with patterns relating to more established biomarkers, but with higher testing rates in the U.S.
- Clinical practice guidelines for PD-L1 in NSCLC were revised in 2017 and now more than 80% of patients are being tested with highly similar rates in both the U.S. and EU4+UK.
- Newer biomarker tests or approaches like tumor mutation burden (TMB), BRAF and RET have greater usage in the U.S., potentially related to the timing of approval of drugs related to those biomarkers compared to EU4+UK, while T790M, a mutation of EGFR has higher testing in EU4+UK than the U.S.
- Melanoma has more consistent BRAF testing rates across countries while differences are larger in other biomarkers and especially micro-satellite instability (MSI).
- Colorectal cancer (CRC) biomarker testing differs significantly across the countries, most notably with PD-L1 testing at only 5% in EU4+UK compared to 56% in the U.S.
- Testing rates in EU4+UK for TMB and MSI, which often suggest the applicability of tissue agnostic checkpoint inhibitors, have lagged behind the rates in the U.S. as there have not been guidelines and drugs have received tissue-agnostic indication approvals later than in the U.S.

Notes: NSCLC= Non-small cell lung cancer, CRC= Colorectal cancer, CLL= Chronic lymphocytic leukemia.

Use of checkpoint inhibitors has risen rapidly in major markets with variations on a per capita basis and some lagging

Exhibit 35: Immuno-oncology checkpoint inhibitor treated patients per 100k population, 2016–2026



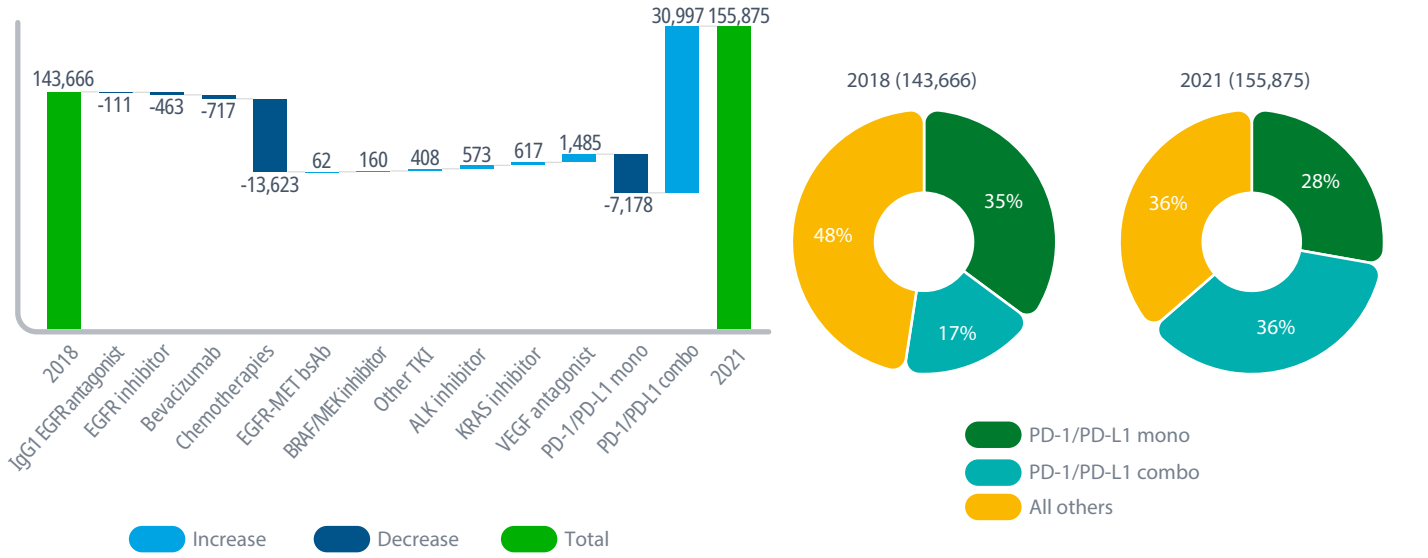
Source: IQVIA Oncology Link, World Bank Population Estimates, Dec 2021.

- The wide adoption of immuno-oncology checkpoint inhibitors reflects their strong efficacy across a range of solid tumors, including several with tissue-agnostic approvals triggering their use with biomarker testing results.
- Usage has varied considerably across countries, with the U.S., France and Japan using almost three times more of these drugs per capita than smaller European markets.
- Many of the major European countries have highly similar rates of usage to other developed markets, including the Nordic countries.
- Use of these medicines is influenced by the use of biomarker testing as well as the position in protocols, where the drugs are progressively moving to earlier lines of therapy with longer treatment durations.

Notes: Volumes of each drug have been normalized based on standard dosing to a day of therapy. Days of therapy per capita are compared across countries. Analysis does not reflect real-world patient usage and dosing of these medicines.

Non-small cell lung cancer treatment has shifted to include checkpoint inhibitors as the standard of care in the past 3 years

Exhibit 36: U.S. advanced/metastatic non-small cell lung cancer treatment regimens, 2018–2021



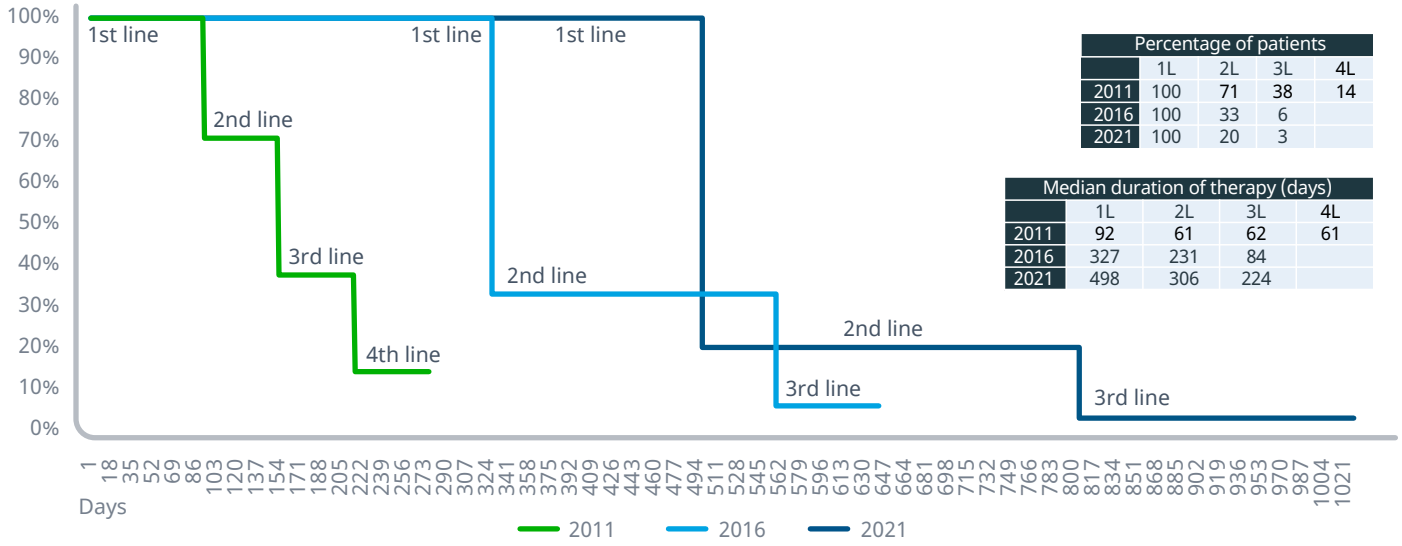
Source: IQVIA Anonymized Patient Claims Data, projected, Dec 2021.

- There have been significant changes in treatment regimens for advanced non-small cell lung cancer in the past three years as more novel therapies have entered the market.
- The total number of patient treatment regimens has increased 8% since 2018, driven largely by significant growth in the use of PD-1/L1 drugs in combination with other therapies.
- Significant declines have been seen in monotherapy PD-1/L1 regimens as patients are switched to combination therapies having greater efficacy, with 28% of treatment regimens for monotherapy PD-1/L1 in 2021 (down from 35%) compared to 36% for combination PD-1/L1 therapies in 2021 (up from 17%).
- As PD-1/L1 checkpoint inhibitors have become more standard of care for patients with advanced non-small cell lung cancer, older non-targeted chemotherapies have seen a significant decline in the last three years, with nearly 14,000 fewer treatments in 2021.
- Other targeted therapies are also seeing a rise in usage, such as VEGF antagonists, KRAS inhibitors and bispecific antibodies, highlighting the availability of a variety of targeted therapies for those with non-small cell lung cancer.

Notes: Estimated patients are based on projected medical claims and regimen clusters have been defined to be non-overlapping. Where a regimen includes multiple elements shown on the chart, a sequence has been used to report regimens containing PD-1/PD-L1 before considering others.

Significant advances, primarily in immunotherapy, have extended median duration of first-line therapy with more responding

Exhibit 37: Non-small cell lung cancer duration of therapy by line of therapy



Percentage of patients	1L	2L	3L	4L
2011	100	71	38	14
2016	100	33	6	
2021	100	20	3	

Median duration of therapy (days)	1L	2L	3L	4L
2011	92	61	62	61
2016	327	231	84	
2021	498	306	224	

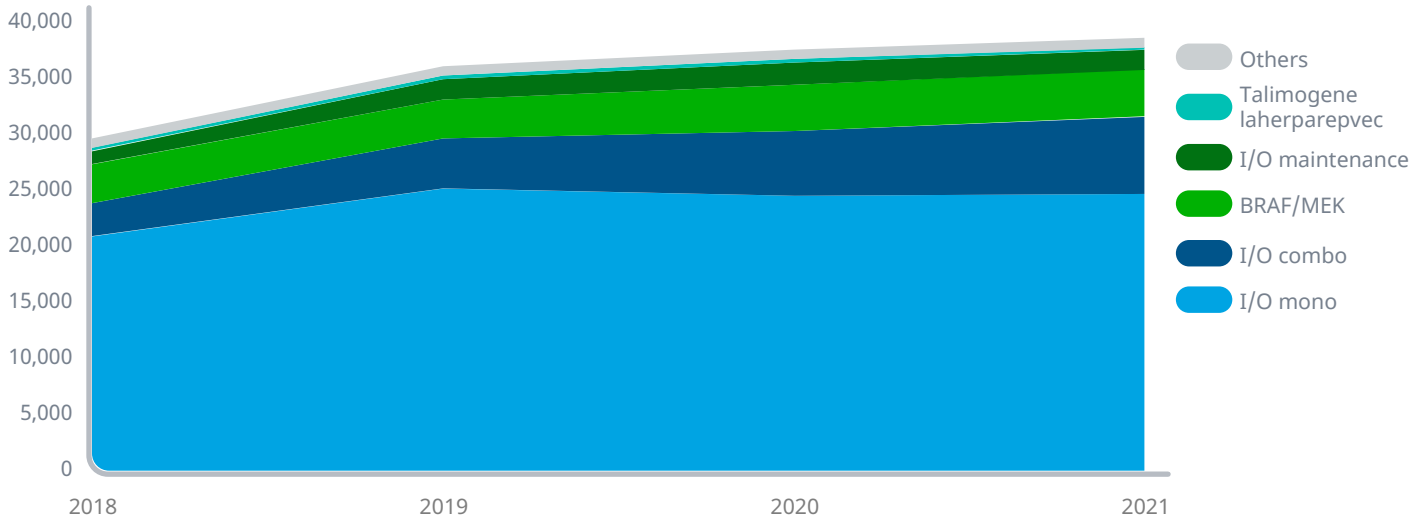
Source: IQVIA Institute, Apr 2022.

- Significant improvements in therapies for non-small cell lung cancer have increased the effectiveness of first-line therapy in patients over the last decade.
- The median duration of first-line therapy has quadrupled since 2011 and now first-line therapy duration is at nearly a year-and-a-half compared to just three months a decade ago.
- In addition to longer durations of therapy for first-, second- and third-line therapies, the percentage of patients responding to each line of therapy has dramatically increased, with only 20% of patients progressing to second-line therapy in 2021 compared to 71% in 2011.
- These improvements can also be seen in those responding to second-line therapies, with only 3% progression to third-line therapies compared to 38% a decade ago and a significant number of patients historically requiring fourth-line therapy.
- This highlights significant improvements in the standard of care and prognosis for patients living with non-small cell lung cancer, driven by innovative targeted therapies such as immunotherapies.

Notes: Vertical axis of the chart represents the percentage of patients on the noted line of therapy. Horizontal axis represents days duration of the relevant line of therapy.

Melanoma is treated with immuno-oncology checkpoint inhibitors 80% of the time with rising use of combo regimens

Exhibit 38: Number of patient treatment regimens in the U.S., 2018–2021

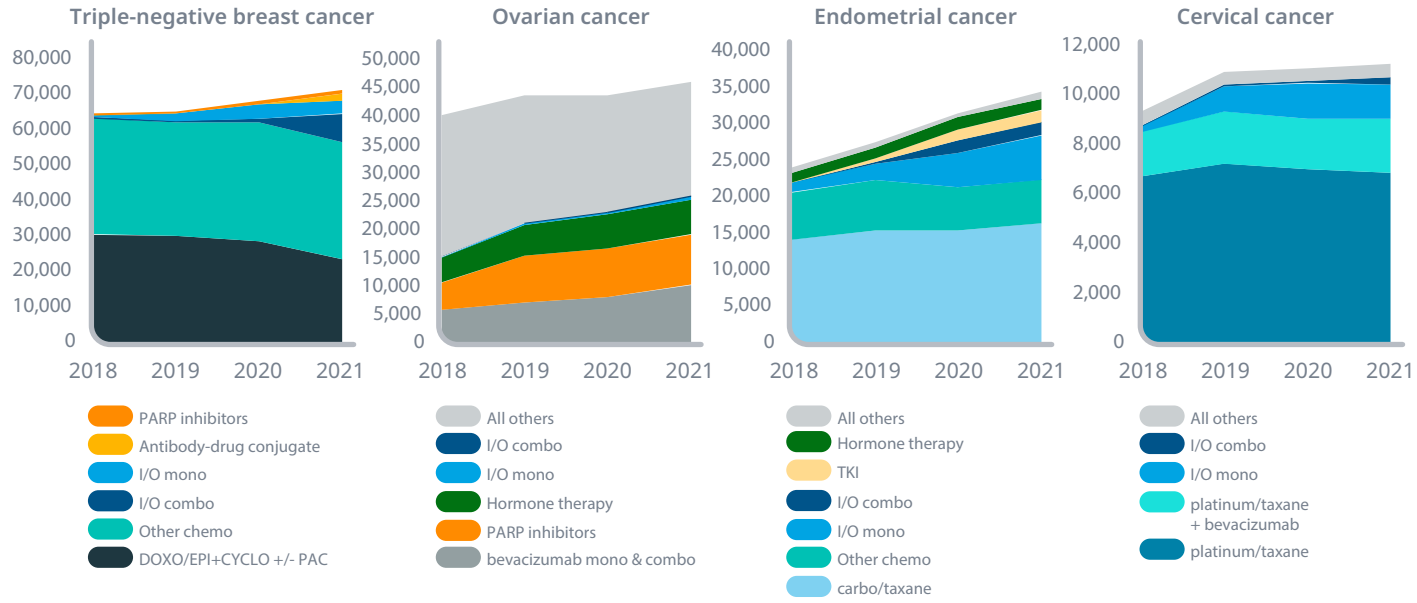


Source: IQVIA Anonymized Patient Claims Data, projected, Dec 2021.

- Treatments for melanoma have been increasing over the last three years, with 30% growth in the number of treatment regimens since 2018.
- Immuno-oncology checkpoint inhibitors play an important role in the treatment of melanoma with monotherapy immuno-oncology checkpoint inhibitors being the most common treatment regimen used for melanoma, accounting for 64% of treatments in 2021.
- Immuno-oncology checkpoint inhibitors are increasingly used in combination with other drugs though, with checkpoint inhibitor combination treatment regimens more than doubling since 2018 and now representing 18% of treatments (up from 10%).
- Combination therapies with BRAF and MEK inhibitors continue to account for approximately 10% of treatments for melanoma, not surprising given that half of melanomas contain BRAF mutations making them susceptible to these therapies.[6]

Immunotherapies and PARP inhibitors have shifted treatment patterns in cancers affecting women especially in the last 2 years

Exhibit 39: Number of patient treatment regimens in the U.S., 2018–2021



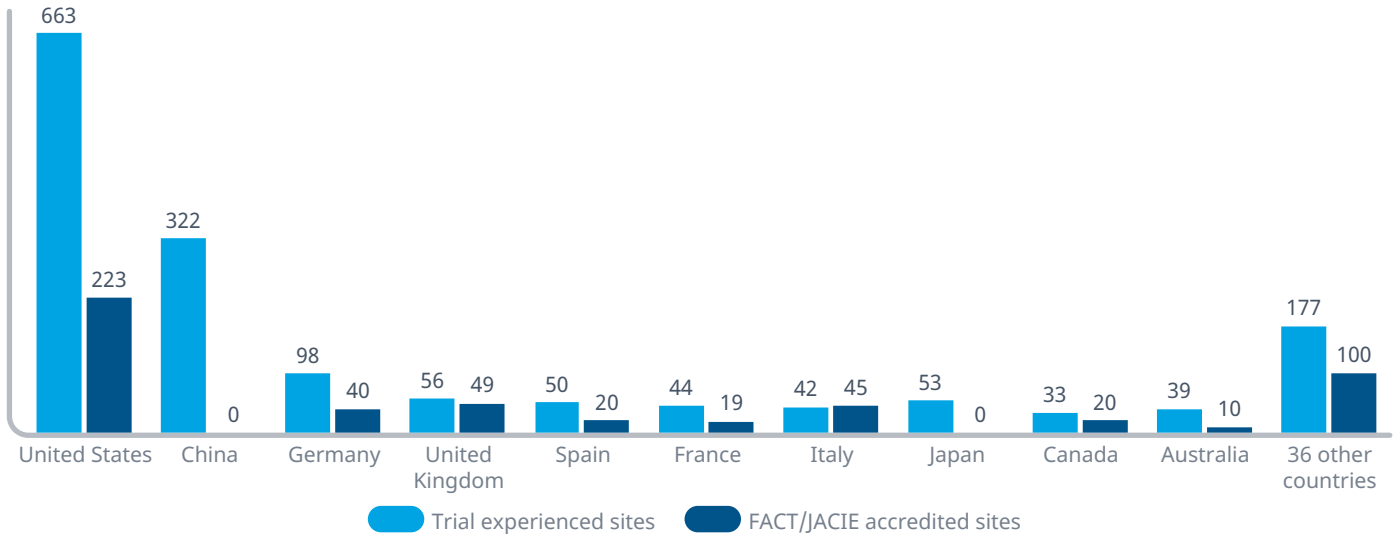
Source: IQVIA Anonymized Patient Claims Data, projected, Dec 2021.

- The overall number of patient treatment regimens has been growing strongly across a range of tumors affecting women.
- Much of the growth in treatment in the past four years has been driven by adoption of newer medicines with notably better clinical outcomes.
- Triple-negative breast cancer, a version of the disease with few options just a few years ago, has seen wider use of checkpoint inhibitors both alone and in combination regimens.
- Antibody-drug conjugates are increasingly being used in breast cancer and will become more widely used in the next several years, driven by greater efficacy and the specificity in delivering a chemotherapy payload to the tumor.
- Ovarian cancers have been relatively hard to treat but cost reductions from biosimilar bevacizumab, which is a component of the most widely used regimen, have benefited some patients.
- PARP inhibitors launched in the last decade have become a backbone of treatment in ovarian cancer, while checkpoint inhibitors are less widely used.
- Endometrial cancer has seen a dramatic rise in the use of checkpoint inhibitors both alone and in combination regimens along with small molecule kinase inhibitors (TKI).
- Cervical cancer treatment has seen a dramatic uptake of checkpoint inhibitors in the last few years, which like other tumors is benefiting from their substantial efficacy and tolerability.

Notes: Regimens are non-overlapping and have been defined with the named medicines or clusters of drugs in a sequence, thus regimens that include other medicines are included but shown in the 'other' categories.

There are 526 hospitals accredited with international standards for the administration of CAR T therapies globally

Exhibit 40: Number of research sites or treatment hospitals with CAR T capabilities by country, May 2022

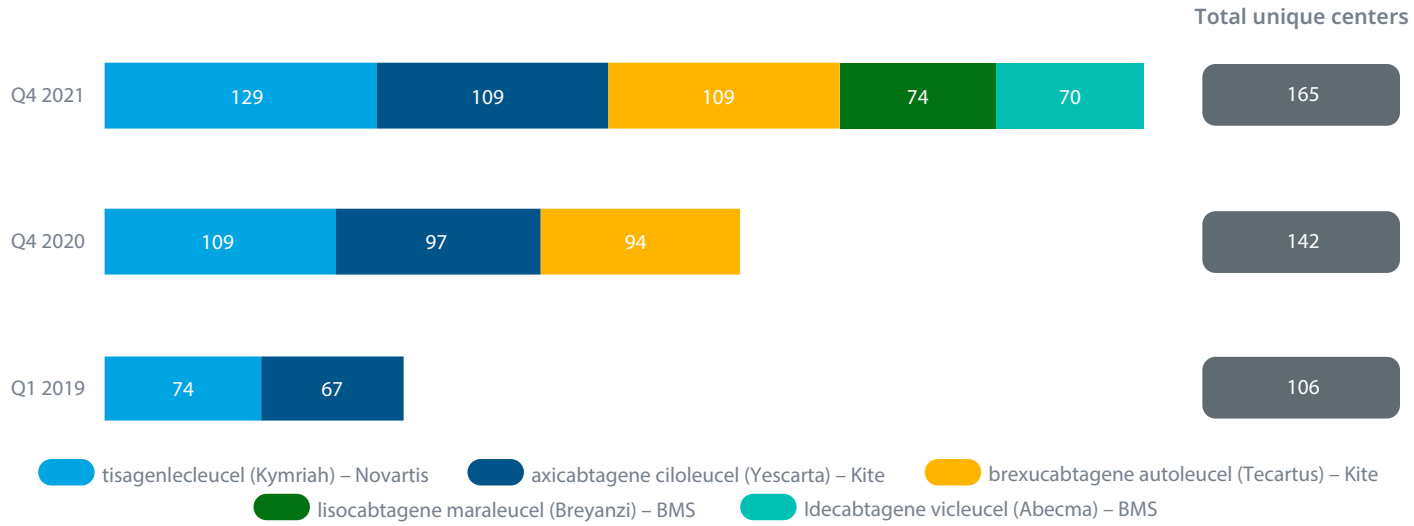


Source: Citeline Trialtrove, IQVIA OneKey, May 2022.

- Administering CAR T cell therapy is relatively complex, such that only a subset of cancer centers are trial-experienced or accredited to deliver these treatments.
- There are 1,577 trial experienced sites globally, including 322 in China, where a large amount of innovation in CAR T cell research is taking place.
- There are many more hospitals which have participated in clinical trials for CAR T cell therapies than have accreditation to deliver them, suggesting that in the future these therapies can become much more accessible and widely used.
- The number of accredited sites grew from 386 in 2020 to 526 in 2021, indicating the increase in approved CAR T cell therapies and increased access for patients. Over 40% of the accredited sites are in the U.S. and none are accredited in China.
- To date, the accredited and administering sites are generally located at or near teaching hospitals or research centers, in areas where there is a sufficient catchment area to provide patient pools, or they are near enough to transport links to enable patients to travel.
- The extent to which centers in more remote or less populated areas offer these treatments will depend on the kinds of investments required, which could be mitigated if a greater degree of standardization across therapies emerges.
- While accreditation[7] is not required to administer these therapies, in developed countries it is a widely accepted standard and all of the actively administering sites in the U.S. are accredited.

While the number of CAR T cell centers is growing, not all centers have all approved products available

Exhibit 41: U.S. CAR T cell center growth (by product)



Source: IQVIA CAR T Cell Monitor, Date updated Dec. 20, 2021.

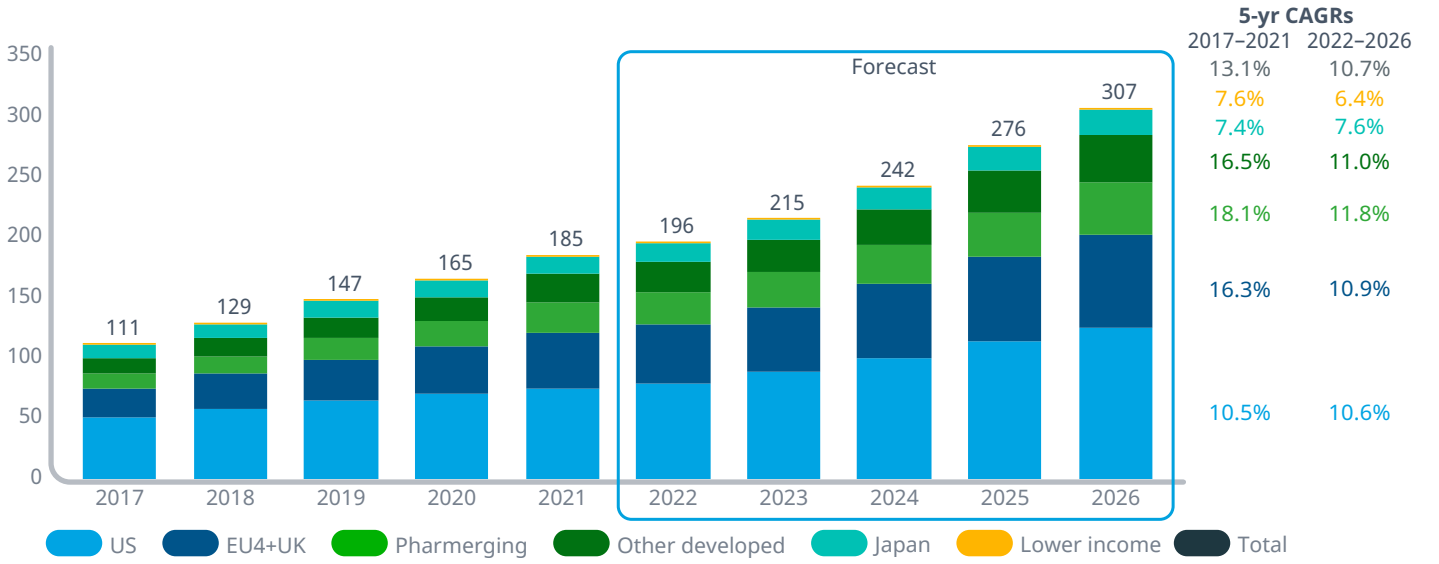
- Despite significant growth in the number of centers providing CAR T cell therapies to patients, not all centers are currently offering each approved therapy.
- Brexucabtagne autoleuel (Tecartus), which launched in July 2020, was picked up quickly and was in two-thirds of active centers by the end of 2020, similar to axicabtagene ciloleucel (Yescarta) which has been approved since 2017, however this remained unchanged by the end of 2021.
- Lisocabtagene maraleucel (Breyanzi) and idecabtagene maraleucel (Abecma), both approved in 2021, were only offered in roughly 40% of centers by the end of the year.
- Given that idecabtagene maraleucel (Abecma) was the only approved CAR T cell therapy for multiple myeloma this could create difficulties for patients with advanced disease who may not live near a center that offers the product and will be important to track in 2022 with the launch of ciltacabtagene autoleucel (Carvykti), which also treats multiple myeloma.
- Given the difference in products and indications, certain products only being offered at select centers could create challenges requiring patients to travel long distances to receive therapies and creating inequities for those who may not have the resources to travel.

Spending on oncology medicines

- Global oncology spending growth to exceed $300Bn by 2026, with growth rebounding with innovation after biosimilar events.
- Cancer medicine spending rose to $185Bn globally in 2021 and is expected to reach more than $300Bn by 2026.
- Growth in major markets is driven by new products and brand volume, and offset by losses of exclusivity, including biosimilar impact.
- China oncology spending now exceeds the rest of pharmerging countries driven by new therapies, brand volume and generics.
- Oncology spending growth in China is expected to return to double digits by 2026 following a slow down in 2022.
- Seven of the top ten tumors have double-digit spending growth, all areas of significant numbers of breakthrough new medicines.
- 69% of oncology launches had annual costs above $100,000 in the past five years, up from 51% in the prior five years.
- Together, PD-1/L1 inhibitors are used across most solid tumors, with 45% of spending for lung cancer in 2021.
- The outlook for next-generation biotherapeutics in oncology includes significantly uncertain clinical and commercial success.

Cancer medicine spending rose to $185Bn globally in 2021 and is expected to reach more than $300Bn by 2026

Exhibit 42: Oncology spending by region, US$Bn



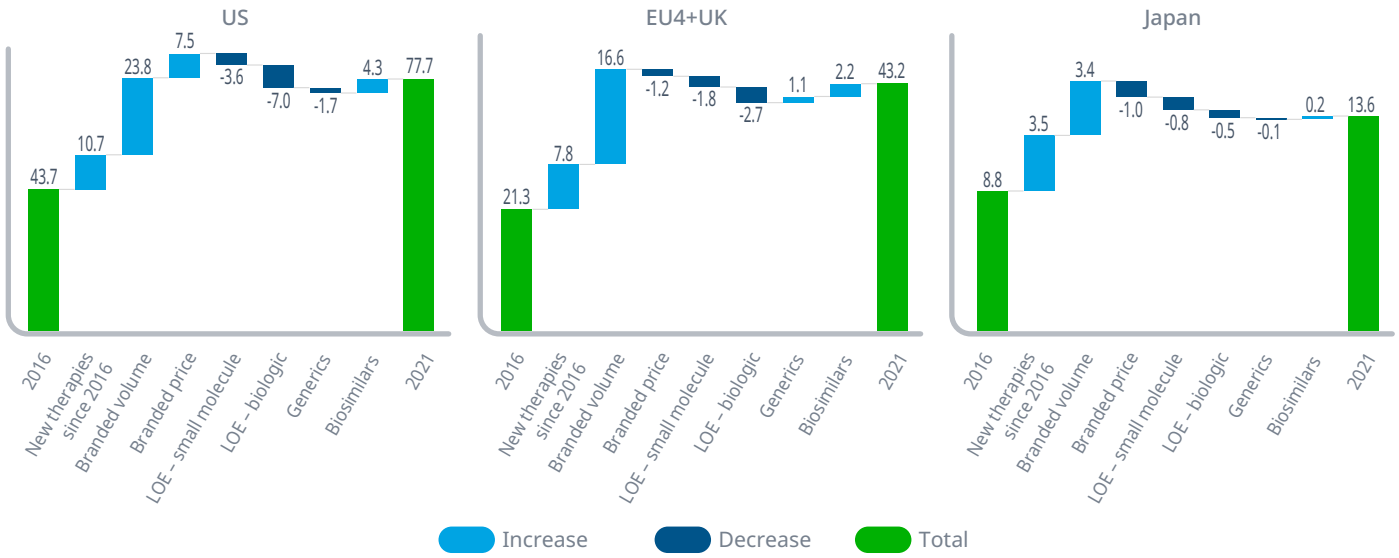
Source: IQVIA Oncology Link, Apr 2022.

- Cancer medicine spending rose to $185Bn globally in 2021, with 74% focused in the major developed markets (the United States, EU4+UK and Japan) down from 77% in 2017.
- Spending growth in these major developed markets is expected to be similar in the next five years to the last five, with the exception of EU4+UK, which is expected to slow.
- The U.S. spending has risen from $50Bn in 2017 to $75Bn in 2021, representing 41% of global spending, down from 45% in 2017.
- Growth in the U.S. is expected to remain in the 9-12% range as the availability of biosimilars for bevacizumab, trastuzumab and rituximab contributed to slowing growth through 2021, and new drugs targeting more niche and rare cancer targets will limit sales uptake in the coming years.
- Wider healthcare access in pharmerging and lower-income countries in the rest of the world lifted spending there, with total spending across these countries of $25Bn in 2021 representing 14% of global spending, up from 11% in 2017.
- Other developed countries accounted for $23Bn of spending in 2021, expected to grow at a rate of 10–13% through 2026, slower than the 16.5% five-year growth through 2011, as biosimilars and less contribution from new drugs are expected to slow growth.

Notes: Pharmerging are defined as countries with less than $30,000 per capita income and more than $1Bn in five-year market growth (covering all drugs, not solely oncology). Other developed countries are those with per capita incomes above $30,000. Lower income are those with per capita incomes below $30,000 but without substantial pharmaceutical market growth.

Growth in major markets driven by new products, brand volume and offset by losses of exclusivity, including biosimilar impact

Exhibit 43: Spending and growth drivers constant US$Bn, 2016–2021



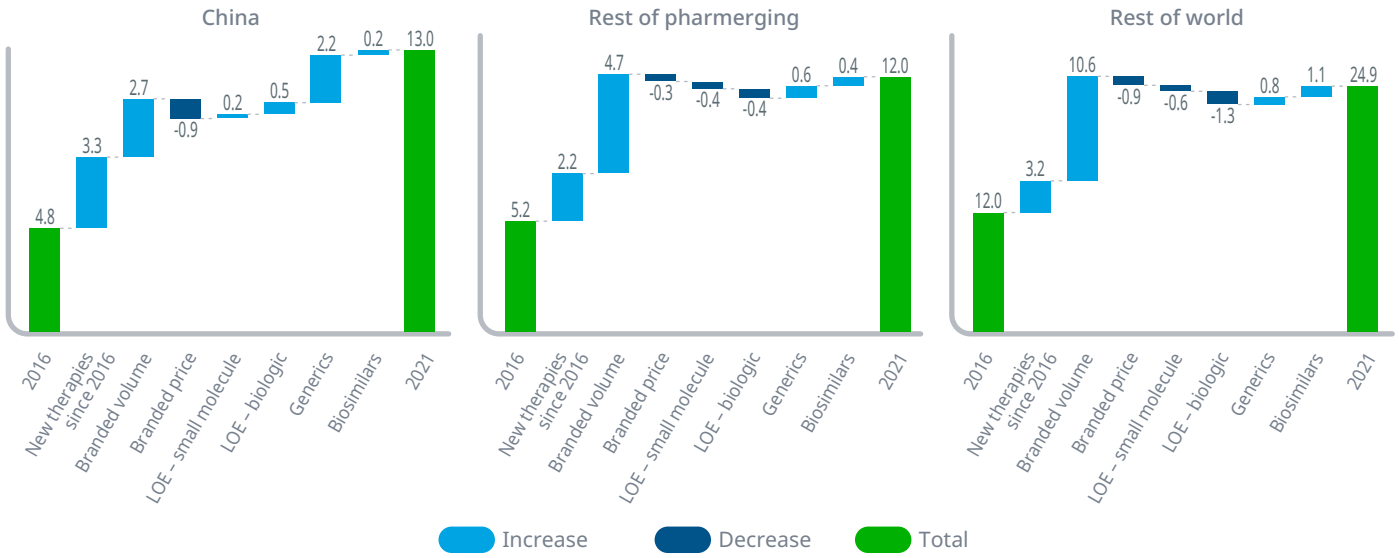
Source: IQVIA Oncology Link, Apr 2022; IQVIA MIDAS, Dec 2021.

- Growth in the last five years in the global oncology market totaled $85Bn, with $30.5Bn of growth from the U.S.
- Growth in the U.S. was driven by new products and the wider use of earlier-launched drugs, especially immuno-oncology checkpoint inhibitors, some of which launched in 2016 or earlier.
- Price growth, long a unique feature of the U.S. market, has reduced dramatically in recent years, while biosimilar impact has begun to impact the market substantially since 2019.
- Europe has experienced very similar growth trends, while notably the oncology biosimilar uptake measured at list prices likely masks the degree of lower negotiated contract and tender prices in these countries.
- Japan's biennial price cut system, including incremental price cuts for products which exceed volume forecasts, has dampened the sales growth from newer drugs, including checkpoint inhibitors, which initially outperformed expectations. Price cuts may shift to annual frequency as a further dampening impact on growth.
- In total, these leading markets have grown by $59Bn over the past five years, accounting for 69% of global growth in that period.

Notes: Product segments are mutually exclusive in each period. New brands since 2016 show the total 2021 spending for all new branded products launched since the end of 2016. New brands include both novel active substances and other brands which may be reformulations or line extensions of earlier NAS launches. Branded volume and branded price are based on protected brands, which are defined as those products with patent protection still in force, and in this analysis excluded all branded products that are new since 2016. Price growth is the impact on growth of changes to invoice prices tracked in IQVIA audits if volume is held constant. Volume growth is the impact on growth if prices are held constant. LOE (loss of exclusivity) is defined as the growth for branded products after they lose exclusivity, typically after patent expiry. Generics include all non-original products including unbranded generics and non-original branded products such as branded generics or company branded products.

China oncology spending now exceeds the rest of pharmerging countries driven by new therapies, brand volume and generics

Exhibit 44: Spending and growth drivers constant US$Bn, 2016–2021



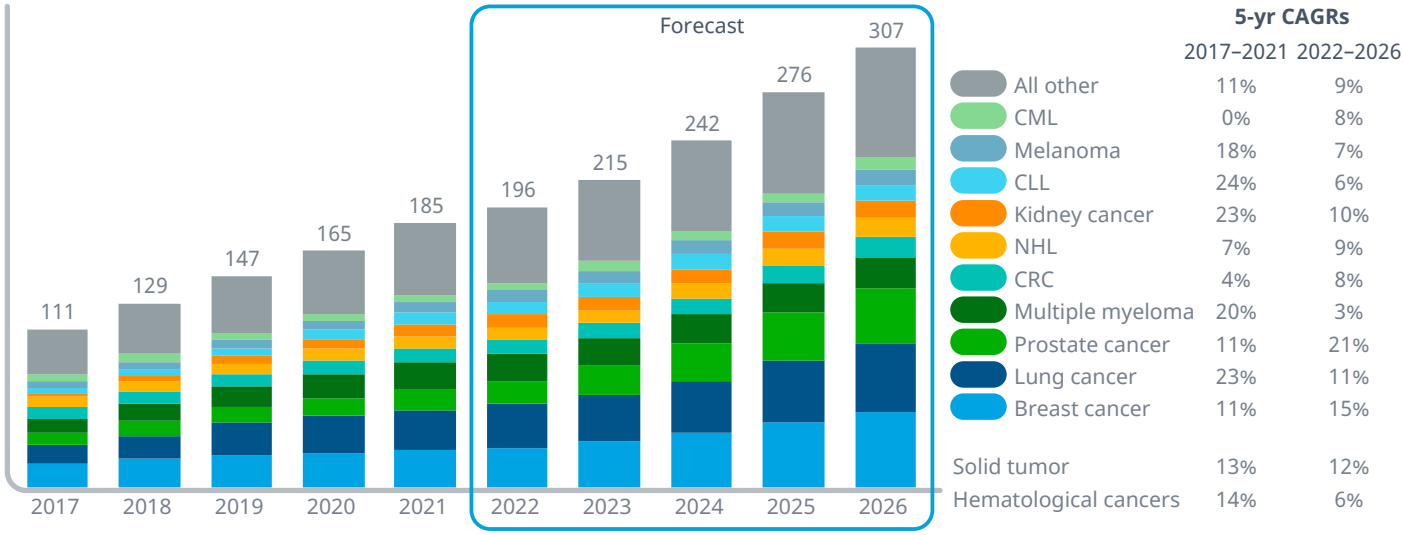
Source: IQVIA MIDAS, Dec 2021.

- China oncology spending grew by $8.2Bn since 2016, with wider access to novel global medicines, a burgeoning home-grown research-based sector and wider use of existing medicines including generics.
- The other 20 pharmerging countries in total grew by $6.8Bn over five years, with positive growth from new drugs and more volume from existing protected brands. These drivers were offset by price declines and the impact of patent expiries.
- In the remaining countries in the world, a mix of developed and lower income markets, most of the growth has been driven by new drugs and wider use of slightly older medicines, most often the checkpoint inhibitors and therapies launched just prior to 2016.

Notes: Product segments are mutually exclusive in each period. New brands since 2016 show the total 2021 spending for all new branded products launched since the end of 2016. Branded volume and Branded price are based on protected brands, which are defined as those products with patent protection still in force, and in this analysis excluded all branded products that are new since 2016. Price growth is the impact on growth of changes to invoice prices tracked in IQVIA audits if volume is held constant. Volume growth is the impact on growth if prices are held constant. LOE (loss of exclusivity) is defined as the growth for branded products after they lose exclusivity, typically after patent expiry. Generics include all non-original products including unbranded generics and non-original branded products such as branded generics or company branded products. Rest of World includes all audited countries outside pharmerging, U.S., EU4+UK and Japan.

7 of the top 10 tumors have double-digit spending growth, all areas of significant numbers of breakthrough new medicines

Exhibit 45: Global oncology spending by tumor US$Bn, 2017–2026



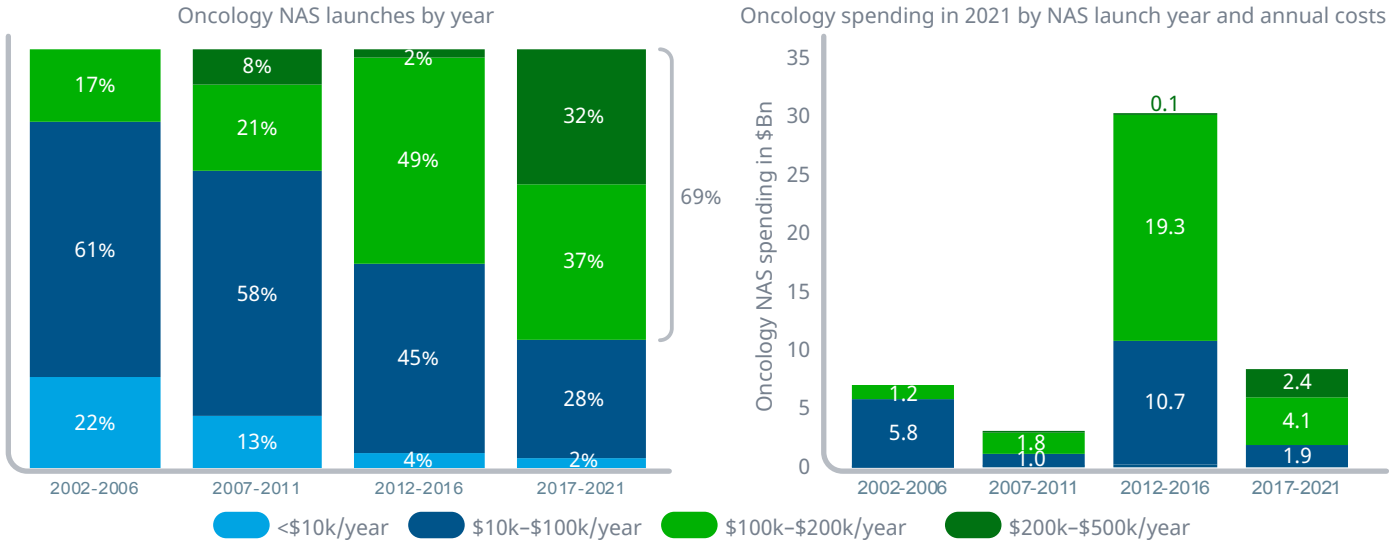
Source: IQVIA Oncology Link, Apr 2022.

- Collectively, the top five tumor types (breast cancer, lung cancer, multiple myeloma, prostate cancer and colorectal cancer), account for 53% of all oncology sales.
- The continued launch of innovative medicines is one of the key drivers fueling the growth in oncology (see exhibits 8 and 9).
- The high value growth observed in NSCLC, melanoma, kidney cancer and SCLC can be attributed to the launch of PD-1/L1 Inhibitors in these patient groups. Prior to the launch of this class of products, targeted therapy options were limited in a few of these cancer types.
- Slower value growth is observed in colorectal cancer and non-Hodgkin lymphoma where the proportion from recent novel active substance contribution is also lower.
- Growth is expected to slow in several tumor types as growth shifts from newly treatable patients to earlier lines of therapy and adjuvant settings in some cases.
- Longer treatment durations and more cycles of therapy per patient contribute to spending growth directly as well as through the continued spending on medicines which are included in regimens with more novel therapies.

Notes: Spending is for medicines only and does not include medical costs or supportive care.

69% of oncology launches had annual costs above $100K in the past 5 years, up from 51% in the prior 5 years

Exhibit 46: Oncology NAS launches in U.S. 2002–2021 by annual costs and sales



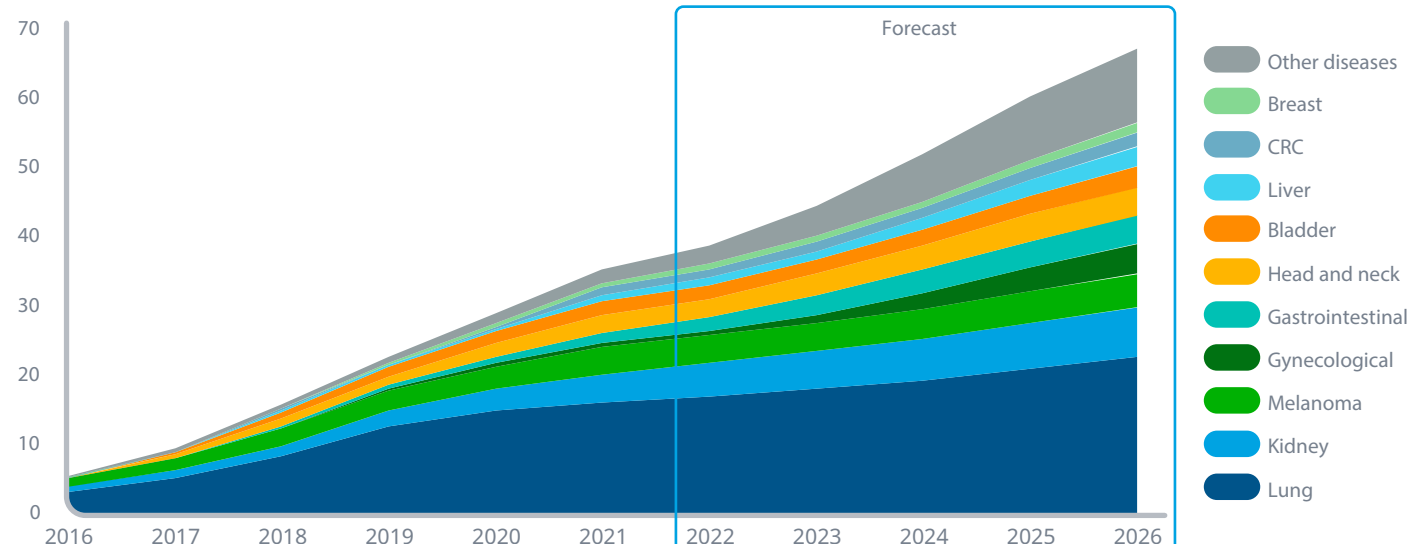
Source: IQVIA Institute, Apr 2022.

- The number of new cancer drugs with costs to the U.S. health system exceeding $200,000 per year has been increasing, accounting for 32% of launches in the past five years, up from 2% in the prior five years.
- Novel cancer drugs with costs above $100,000 were 69% of launches in the past five years up from 51% in the prior five years.
- High-cost therapies totaled $29Bn of spending in 2021, with $23Bn from launches in the past ten years.
- While individual drugs can have a high cost, the cost of a patient's treatment continues to vary based on the overall regimens they receive and non-drug components of their care and can especially be influenced by their insurance type.

Notes: Annual costs are based on standard dosing in the most common indication approved in the launch year of the drugs. Costs do not include other components of the treatment regimen or non-drug costs. Costs are total costs at list prices most often sourced from company statements or derived from IQVIA data and the approved label dosing. Where dosing is based on body weight, surface area or other variables, U.S. national averages have been used. Gender-specific or age-range specific assumptions are included if required.

Together, PD-1/L1 inhibitors are used across most solid tumors with 45% of spending for lung cancer in 2021

Exhibit 47: Global PD-1/L1 inhibitor sales by tumor type, constant US$Bn

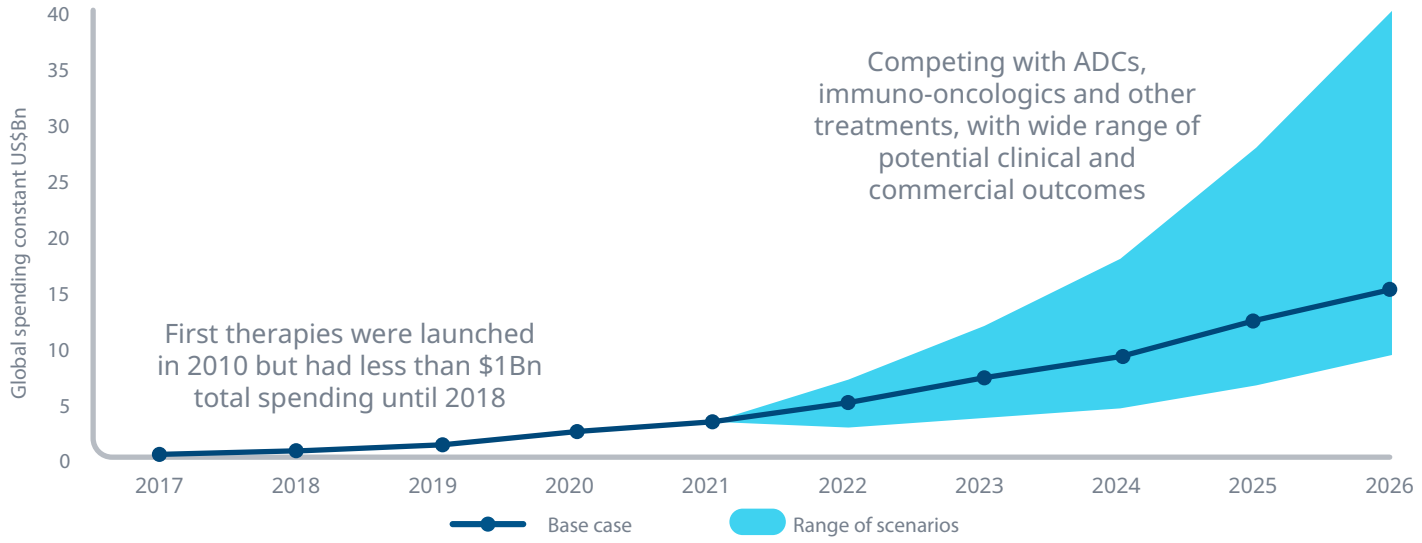


Source: IQVIA Oncology Link, Apr 2022.

- Immuno-oncology products represent a key class that has revolutionized cancer treatment across a spectrum of indications.
- Checkpoint inhibitors, mainly the PD-1/L1 checkpoint inhibitors, have impacted clinical practice the most to date and account for $35Bn in global spending in 2021, up from $5.6Bn in 2016.
- The largest PD-1/L1 segments today are NSCLC followed by melanoma and kidney cancers and including dozens more as key PD-1/L1s have been approved as "tissue-agnostic," where a biomarker test result indicates use, regardless of the specific solid tumor.
- Some of the fastest growing indications are small cell lung cancer (SCLC) and bladder cancer where usage is shifting to earlier lines of therapy.
- Looking ahead, many PD-1/L1 inhibitors are being used as combination therapies with other molecules as they're becoming backbone treatments in certain tumor types and this trend is expected to continue.

The outlook for next-generation biotherapeutics in oncology includes significantly uncertain clinical and commercial success

Exhibit 48: Cell, gene and RNA therapeutics



Source: Company Financials, IQVIA Institute, Nov 2021.

- A range of therapies have been grouped together as next-generation biotherapeutics, reflecting a variety of cell therapies, gene therapies, gene editing and RNA interference or modification technologies, most of which had no marketed drugs a decade ago.
- Cancer cell therapies have had a limited number marketed for over a decade, and in 2021 totaled $3.6Bn in spending.
- The outlook for these therapies is complex with significant uncertainties related to clinical issues such as efficacy, durability of response and safety.
- Scenarios with higher overall spending could result if concerns are unwarranted and expected numbers of these drugs reach the market, receiving relatively wide reimbursement and usage. This could result in a large spending contribution driving a high-end scenario of $40Bn in spending a year.
- These next-generation therapies will compete with other novel agents, where selection of a treatment for a patient may include decisions about efficacy, tolerability and potentially cost.
- The combination of these factors contribute to the base-case outlook for growth to $15Bn in global spending by 2026, substantially below the high-end scenario but reflecting the range of unknowns surrounding this groundbreaking research.

Notes: Historic values derived from company financials for marketed therapies. Estimates of future spending based on IQVIA estimates of numbers of future launches and expected continued uptake of existing therapies.

Notes on sources

THIS REPORT IS BASED ON THE IQVIA SERVICES DETAILED BELOW

IQVIA™ PIPELINE INTELLIGENCE is a drug pipeline database containing up-to-date R&D information on more than 40,000 drugs and more than 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 more than 130 countries and including more than 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.

IQVIA MIDAS™ is a unique data platform for assessing worldwide healthcare markets. It integrates IQVIA national audits into a globally consistent view of the pharmaceutical market, tracking virtually every product in hundreds of therapeutic classes and providing estimated product spending, volumes, trends and market share through retail and non-retail channels. MIDAS data is updated monthly and retains 12 years of history.

ONCOLOGY DYNAMICS is a syndicated cross-sectional survey that collects patient-level data from a representative panel of physicians and provides quick access to real world data to unravel dynamics in subpopulations and treatment patterns. Oncology Dynamics has geographic coverage across 17 countries including key European, Middle East, Asia, and Latin American markets, and covers more than 180,000 cases per year and over 4,000 specialists.

BRANDIMPACT™ uses a proprietary mobile research model and longitudinal network of more than 400 internet-enabled oncologists and is the only source of continuously-captured physician treatment decisions for the biopharmaceutical industry. The real-time data generated by its information panel of oncologists enables unique insights into physician behavior and the influences on that behavior.

ONCOLOGY LINK includes 10-year drug spending and treated patient forecasts by tumor, country, therapy area and treatment regimens. Analyses are projected to cover the total oncology market in 75 audited countries globally. Projections are based on total drug spending and volume data from IQVIA MIDAS, adjusted with detailed data in 9 key countries where patient treatment data is collected, accounting for c.85% of global oncology market value. Projections are based on treatment regimens including over 300 drugs and 24 tumors.

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

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, 31,396 distinct drugs were examined, for 125,584 potential phase transitions for events from 1977 to present. We then limited to products where the phase transitions completed between 2010 and 2021, with valid information regarding phase transitions, either successful or failed, which includes 8,669 distinct drugs and 12,403 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).

Phase II trials includes Phases II, I/II, II, IIa and IIb. Phase III includes Phase II/III and III.

Due to unusual and unprecedented events in 2020 and 2021 thought to be related to COVID-19, traditional sources of information for drug development activity have been impacted in ways not consistent with actual drug development activity. In order to assess and adjust for these impacts, a representative sample of medicines otherwise indicated as going inactive in 2021 (following three years of inactivity) were subjected to a more rigorous review. The results of this assessment were applied to 2020 and 2021 Pipeline Intelligence data throughout this report.

Each phase's success rate requires:

- A relevant phase start date and any date occurring afterwards, either positive or negative
- Success is any higher phase with a future date after the phase start date
- Failure is the absence of a successful phase transition and the presence of a discontinued, suspended, withdrawn or inactive event with a date that is after the phase-start date

Invalid entries are excluded for the phases where they are invalid, and a drug can be invalid for some phases and valid for others:

- Drugs which have higher phase entries, but dates are in the past. This can be an artifact of a drug with multiple indications with incomplete information for some of the indications in the source database.
- Drugs which have no higher positive phase dates, but have negative phase dates, but those dates are prior to the target phase start date. This can be an artifact of the original data being indication phase-based.

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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.

MICHAEL KLEINROCK
Research Director, IQVIA Institute for Human Data Science

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.

JAMIE PRITCHETT
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

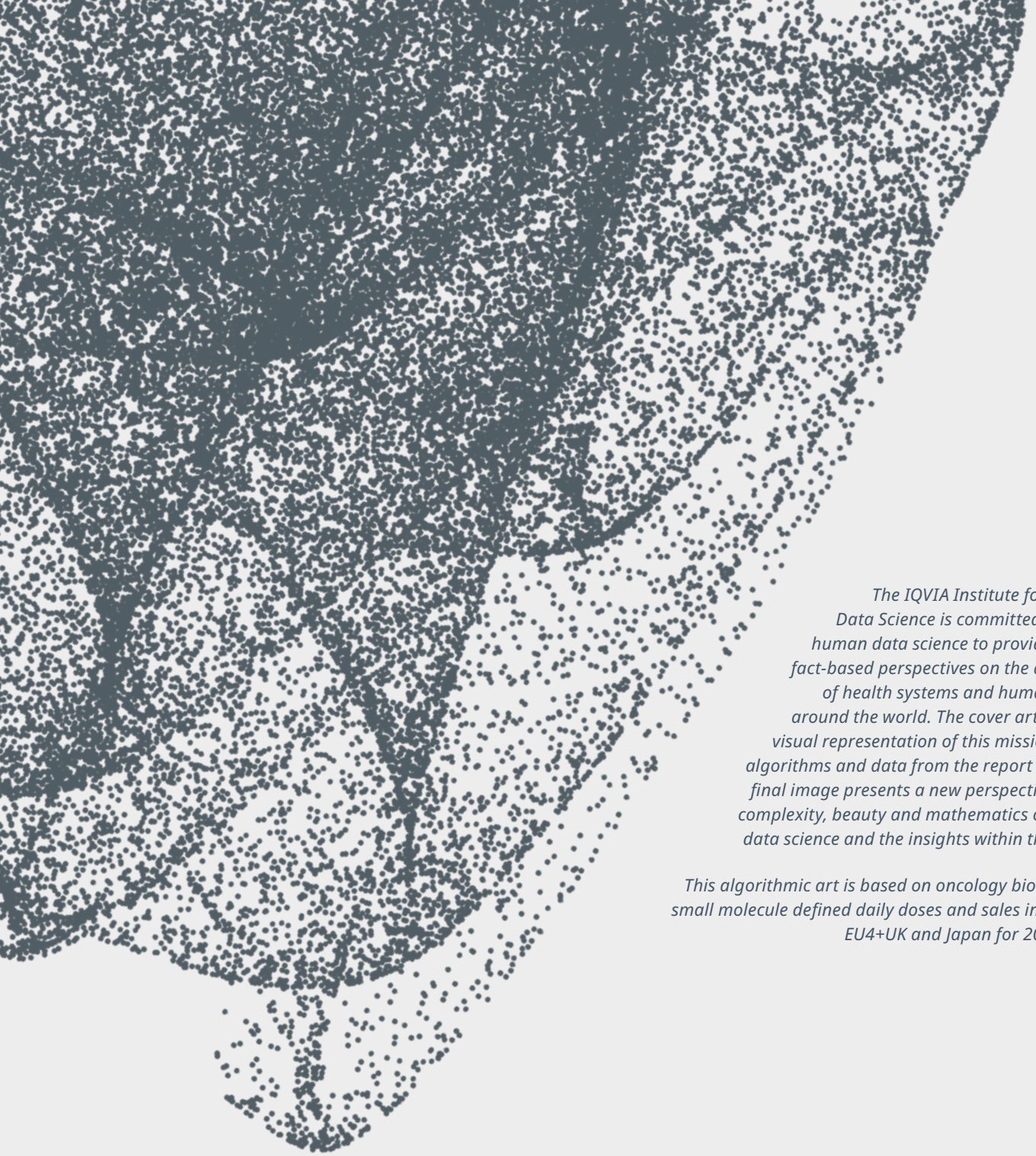
The research agenda for the Institute centers on five areas considered vital to contributing to the advancement of human health globally:

- 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.

This algorithmic art is based on oncology biologic and small molecule defined daily doses and sales in the U.S., EU4+UK and Japan for 2010-2021.

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