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FEBRUARY 9, 2024

PRECISION ONCOLOGY

Global Clinical Trial Landscape (2024)

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PRECISION ONCOLOGY

GLOBAL CLINICAL TRIAL LANDSCAPE (2024)

Precision oncology uses biomarker testing to identify cancer mutations, **improving outcomes with targeted therapy**

Precision oncology utilizes **targeted drug therapy to specifically target cancer cells and immunotherapy** to enhance the body's immune system against cancer

Targeted **therapies involve small and large molecules treating various cancers**, such as angiogenesis inhibitors and monoclonal antibodies.

Immunotherapies include **diverse modalities** (e.g., Checkpoint Inhibitors, CAR T-cell therapy, cytokines, cancer vaccines), which **enhance the immune system against cancer cells, and ADCs** which combine antibodies with drugs for precise cancer cell targeting.

Advances in tumor biology (e.g. breast cancer), led to diverse precision oncology mechanisms

Clinical trials (e.g., cetuximab, pembrolizumab) showcase **targeted therapy success**

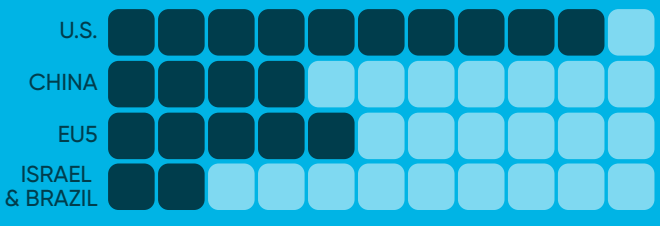
Biomarker-driven strategies (e.g., larotrectinib for NTRK fusions) lead to tumor-agnostic therapy approvals

Precision medicine guides decisions for prevalent cancers: colorectal, breast, lung, leukemia, lymphoma, melanoma, esophageal, stomach, ovarian, thyroid

30% of global oncology trials focused on precision medicine

(2019 to 2023)

- **40%** ASIA-PACIFIC
- **30%** NORTH AMERICA
- **20%** EUROPE
- **10%** ROW



North America, particularly the **U.S., exhibited the highest CAGR**

China led the Asia-Pacific trials (>35%)

EU5 nations led European trials (>45%).

Israel and Brazil each hosted >20% in ROW.

CONTENTS

1. INTRODUCTION

Precision oncology requires the use of biomarker testing to identify the driver mutations of a patient's cancer and actionable biomarkers for targeted therapy treatment (USFDA, American Cancer Society Cancer Action Network). This evolution in oncology treatment is helping to improve patient outcomes with potentially less use of chemotherapy for some cancers such as breast cancer.

The Evolution and Impact of Precision Medicine in Oncology

Precision and personalized medicine refer to a healthcare approach utilizing information about an individual's genes, proteins, and environment for disease prevention, diagnosis, and treatment (NCI, 2023). In cancer, it leverages specific tumor information for diagnosis, treatment planning, assessing treatment effectiveness, and prognosis. The concept of precision medicine originated from the Human Genome Project, which revealed individual genomic variations and laid the foundation for personalized diagnosis and treatment. A fundamental advance was the creation of targeted therapies like imatinib, designed to specifically combat cancer cells by influencing their signalling pathways. Imatinib revolutionized treatments for conditions like chronic myeloid leukemia and expanded to treat various other cancers such as melanoma, breast, lung, and colorectal cancers. The advent of biologics and cellular therapies, like chimeric antigen T cells, offered innovative treatment options, although some associated adverse events were observed.

The benefits of precision medicine were particularly evident in lung cancer treatments. Drugs like lorlatinib, osimertinib, and adagrasib were developed to target specific mutations in non-small cell lung cancer. Skin cancers such as melanoma, showed remarkable responsiveness to immunotherapy, specifically with immune checkpoint inhibitors like nivolumab and ipilimumab (also known as PD-1 inhibitors). For hematologic malignancies like pediatric lymphomas, in addition to conventional drugs, innovative approaches such as gene therapy have been introduced, demonstrating promise with some associated challenges.

Personalized medicine not only revolutionized treatment but also diagnostics. Traditional tumor biopsies, invasive in nature, faced competition from liquid biopsies—non-invasive methods that offer insights into a tumor's genetic makeup. This shift provided clinicians with invaluable prognostic and predictive markers like PD-L1 status. FDA-approved companion diagnostics for specific mutations, such as HER-2 antibodies in breast cancer, further emphasized the role of precision diagnostics.

The rise of personalized medicine prompted innovative clinical trial strategies. Adaptive trials, basket trials, and umbrella trials have emerged, allowing for more targeted patient grouping based on biomarkers. These trial designs not only accelerate drug development but also reduce costs. Consequently, vast amounts of clinical data become available for analysis, with initiatives like KEYNOTE, IMpower, and CheckMate evaluating the efficacy of precision medicine therapies, many of which have now become standard care protocols. [1]

Recent years have seen a transformative change in cancer treatment strategies, marked by the increasing identification of actionable biomarkers and targeted therapies. The integration of cutting-edge genomic profiling technologies has propelled the field of precision oncology, steering away from nonspecific cytotoxic treatments towards more targeted and effective interventions. Over 60 % of cancer drugs authorized by regulatory agencies like the FDA and/or EMA now carry pharmacogenomic labels, reflecting a significant increase in clinically actionable biomarkers. Between 2020 and 2022, over 10 new therapies relying on genomic or molecular alterations were approved. The scope of precision oncology continues to broaden, with new drug modalities expanding therapeutic options across diverse targets and patient populations.

As of November 2023, the FDA has approved twelve treatments for unique biomarker-selected indications, while the NCCN guidelines have incorporated six biomarker and indication-specific treatments in the past year. The momentum towards precision oncology is further emphasized by the inclusion of two therapies as level 3 investigational agents in OncoKB, supported by compelling clinical evidence. This expansion highlights the increasing scope of precision oncology, targeting a broader range of biomarkers and patient populations while minimizing ineffective treatments. [2,3]

This whitepaper explores the global precision oncology trial landscape and various factors influencing precision medicine adoption. It offers a thorough analysis of healthcare, technology, macroeconomic, and regulatory trends, alongside a SWOT analysis, funding, and innovative research developments in precision oncology. Stakeholders, including researchers, clinicians, pharmaceutical and biotech firms will glean valuable insights into the evolving landscape of oncology trials, emphasizing the crucial role of precision medicine in advancing cancer care.

2. PRECISION ONCOLOGY DRUG TYPES

Targeted therapies and Immunotherapies

Precision medicine involves developing treatments precisely designed to target specific changes or substances within cancer cells. Targets may differ among individuals with the same cancer type. After a biopsy or surgery, specific tumor targets are tested, aiding in identifying the most effective treatment. According to *Suehnholz et al., Cancer Discovery 2023*, as specified on OncoKB, precision oncology therapy relies on pre-treatment molecular profiling to identify and optimize patient selection for a drug that is most effective in a molecularly defined patient subset.

Precision oncology commonly employs two primary treatment approaches: targeted drug therapy, which focuses on designing drugs to specifically target cancer cells, and immunotherapy, which utilizes medications to enhance the body's immune system in combating cancer. [4]

Targeted therapies

Small molecule drugs are compact enough to enter cancer cells and block specific substances within the cell. Large molecule drugs are unable to fit into cells and operate by attacking and weakening proteins or enzymes on the cell surface, similar to a "lock and key" mechanism. Various types of cancer can be treated with targeted therapies, each designed to address specific aspects of cancer biology. Examples include angiogenesis inhibitors (e.g., bevacizumab), monoclonal antibodies (e.g., alemtuzumab, trastuzumab, cetuximab), proteasome inhibitors (e.g., bortezomib), and signal transduction inhibitors (e.g., imatinib). [5]

Immunotherapies

Various immunotherapy modalities play crucial roles in cancer treatment, representing a continuously evolving field of research. Examples include Checkpoint Inhibitors like Pembrolizumab and Nivolumab, targeting PD-1 or PD-L1 proteins to bolster the immune system against cancer cells. CAR T-cell therapy involves genetically modifying T cells, illustrated by Kymriah (for B-cell acute lymphoblastic leukemia) and Yescarta (for specific lymphomas). Cytokines, including IL-2 (for advanced renal cell carcinoma and metastatic melanoma), activate immune cells against cancer, while Immunomodulators like Revlimid enhance specific immune components for specific cancers. Cancer Vaccines, like mRNA vaccines, show promise in initiating immune responses in cancer immunotherapy research. Monoclonal Antibodies (e.g., Trastuzumab) and Multispecific Antibodies (e.g., Blinatumomab) target cancer-specific proteins, and Oncolytic Viruses like Talimogene Laherparepvec selectively infect and eliminate cancer cells. Finally, ADCs (antibody drug conjugates, e.g., Ado-trastuzumab Emtansine) combine monoclonal antibodies with cytotoxic drugs, precisely delivering drugs to cancer cells. [6,7]

3. GLOBAL CLINICAL TRIAL LANDSCAPE OF PRECISION ONCOLOGY

From 2019 to 2023, there was a significant upswing in the global oncology trials landscape, marked by the initiation of more than 10,000 trials that were ongoing, of which 30% were specifically focused on precision oncology (trials targeting a specific biomarker in trial subjects). This trend underscores the growing significance of precisely targeted therapies in the field of cancer research.

When considering the regional distribution, the Asia-Pacific region led, hosting 39% of precision oncology trials and providing a dynamic research environment. Following closely, North America contributed 31%, emphasizing its strong role in advancing precision medicine. Europe, with a 21% share, reflected substantial participation in precision oncology research. The Rest of the World (ROW) accounted for 9%, highlighting the global nature of initiatives in precision oncology. (See Figure 1)

Additionally, among the top 3 global regions, North America exhibited a remarkable precision oncology clinical trial growth rate with a 9.5% Compound Annual Growth Rate (CAGR) over the 5-year period from 2019 to 2023. In the Asia-Pacific region, the growth rate stood at 7.3% CAGR, highlighting the continuous progress in precision medicine research. Europe experienced a more modest growth rate at 0.5% CAGR, suggesting a stable but slower advancement in precision oncology trials over the same period. (See Figure 2)

Analyzing trials based on its location, the United States played a central role by conducting 75% of Precision Oncology trials in North America, solidifying its leadership in the advancement of targeted therapies. Canada and Mexico conducted 19% and 6% of trials, respectively, presenting collaborative efforts within the North American region. North America's fastest growth rate in precision oncology trials can be attributed primarily to the Unites States, the country's robust research infrastructure, favourable public and private funding landscape, and a supportive regulatory environment. The United States, with advanced medical facilities and a large pool of skilled researchers, has played a pivotal role in fostering innovation and accelerating the development of targeted therapies. Additionally, streamlined approval processes and the ability to attract top talent have further propelled the rapid expansion of precision oncology trials in the country.

In the Asia-Pacific precision oncology landscape, Mainland China dominated with 36% share, highlighting its key role in advancing precision oncology. South Korea (15%), Australia (12%), and Japan (11%) emerged as the next top contributors, shaping precision medicine landscapes. China's leadership is fuelled by significant investments in healthcare infrastructure, a thriving biotechnology sector, and a sizable patient population. South Korea's leadership is attributed to its advanced medical research environment and a proactive integration of cutting-edge technologies, while Australia's contribution reflects its standing as a leader supported by world-class research institutions, a robust regulatory framework, and a dedicated focus on translational research. Likewise, Japan's efficient regulatory framework facilitates prompt approval of innovative therapies, including those in precision oncology, alongside a strong healthcare infrastructure. The nation's aging population and rising cancer prevalence drive a heightened focus on personalized medicine, leading to increased interest and investment in precision oncology. Collaborative efforts between industry and research institutions, combined with rich patient data resources, further contribute to the growth of precision medicine initiatives in Japan. Additionally, Taiwan, Singapore, Hong Kong, and Thailand together contributed 18%, highlighting the collaborative efforts within the Asia-Pacific region.

In Europe, EU5 nations led precision oncology trials with a 47% share, highlighting their collective commitment to advancing targeted therapies. Rest of Europe (ROE) equally shared the precision oncology research burden with 50%. Russia contributed 3%, showcasing its emerging role in precision medicine research. The EU5 countries lead the precision oncology trials due to their renowned research institutions, clinical expertise, supportive regulatory framework by the European Medicines Agency (EMA), and a diverse patient population. The presence of a thriving pharmaceutical and biotech industry, coupled with well-developed healthcare infrastructures and active international collaborations, further accelerates the region's prominence in advancing precision medicine for oncology.

In the ROW (Rest of the World) region, Israel and Brazil each hosted 22% of precision oncology trials, demonstrating their lead roles in advancing precision medicine. Argentina contributed 17%, while Chile and South Africa played moderate roles with 9% and 8% trials share, respectively, indicating active participation in the regional landscape of personalized cancer treatment studies. The remaining 22% contributed by other countries within the ROW, demonstrates the global nature of precision oncology research. (See figures 3-7)

This comprehensive summary indicates the global and collaborative nature of precision oncology trials, with diverse regions and countries actively contributing to advancing personalized cancer treatments between 2019 and 2023.

Figure 1: Precision oncology trials - % share by region (2019-2023)

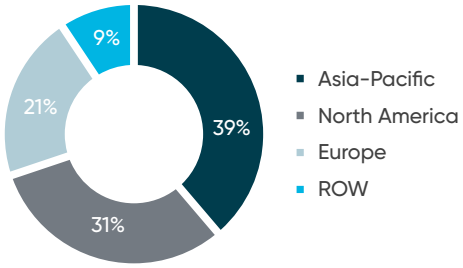


Figure 2: Precision oncology trials - CAGR % by region (2019-2023)

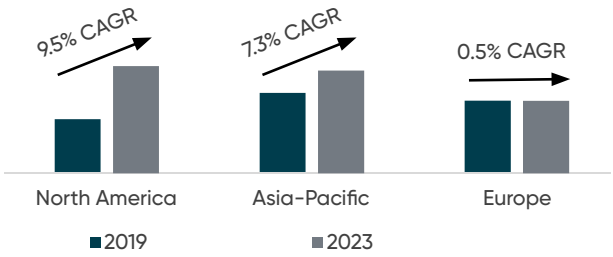
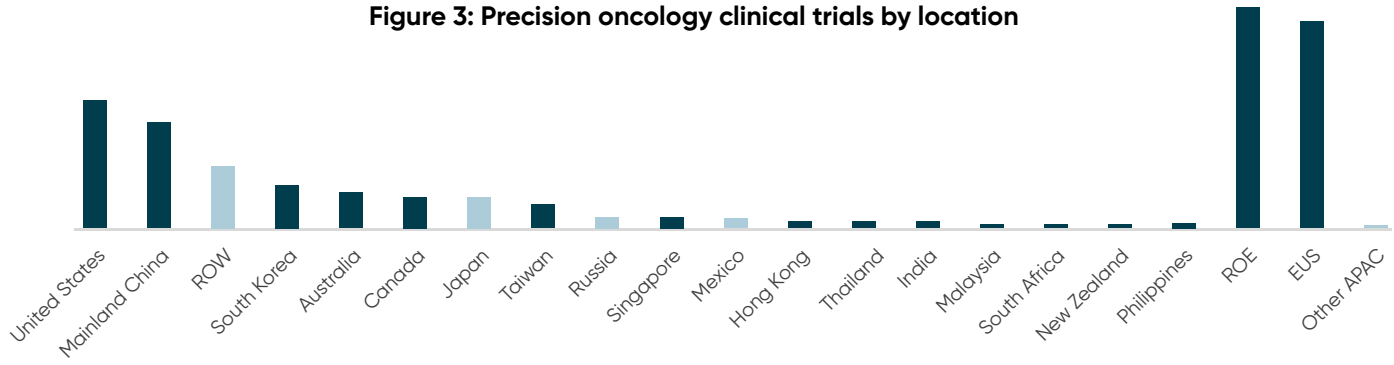


Figure 3: Precision oncology clinical trials by location



Locations where Novotech directly operates; ROE – rest of Europe; EU5 – UK, France, Germany, Spain, Italy; Other APAC: Vietnam, Macau, Afghanistan, Bangladesh, Micronesia, Uzbekistan

Figure 4: APAC trials % share by locations

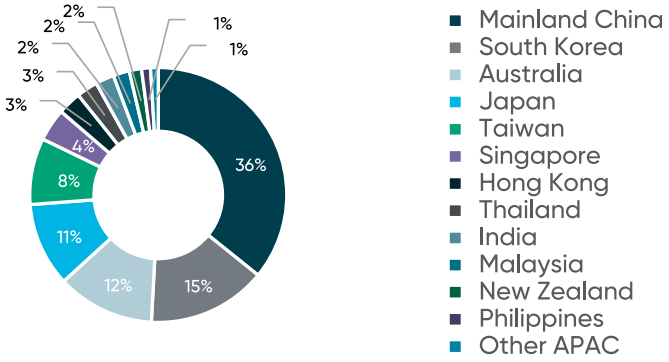


Figure 5: North America trials % share by locations

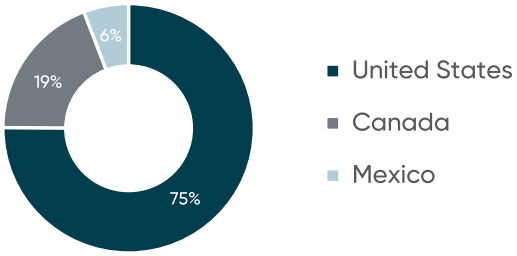


Figure 6: Europe trials % share by locations

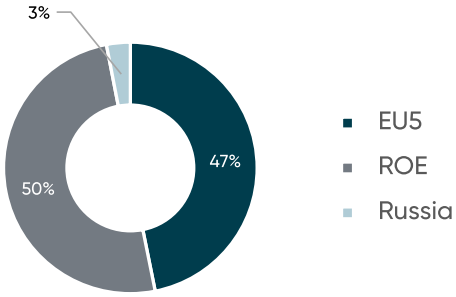
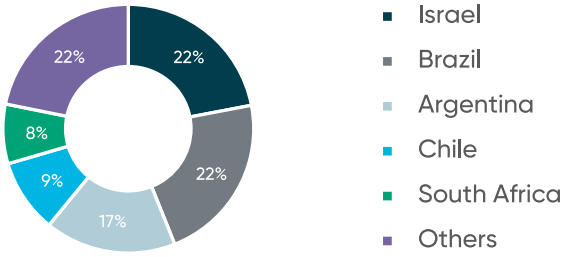


Figure 7: ROW trials % share by locations



Source: GlobalData, January 2024

Patient recruitment landscape of precision oncology trials

In analysing single country precision oncology trials from 2019 to 2023 in the US, Europe, and the Asia-Pacific region, distinct patient recruitment trends emerge. The Asia-Pacific region stands out with the shortest median enrolment period at 19.07 months and the highest median recruitment rate of 0.64 subjects per site per month. This efficiency may be attributed to factors such as a potentially more suitable patient population and higher cancer prevalence in the region. In comparison, the US demonstrates a longer median enrolment period (29.67 months) and a recruitment rate of 0.39 subjects per site per month, while Europe falls in between with a median enrolment period of 26.50 months and a recruitment rate of 0.28. These findings reveal the importance of considering regional nuances for refining precision oncology trial designs and recruitment strategies. (see Figures a and b)

Figure a: Enrolment Period (months)

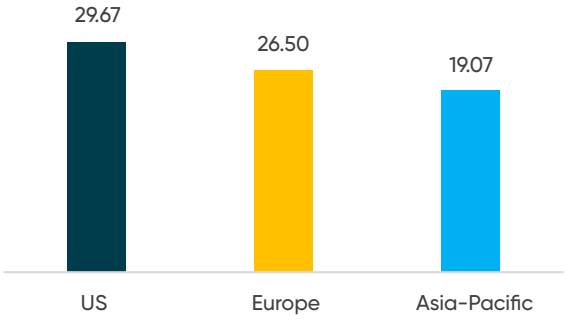
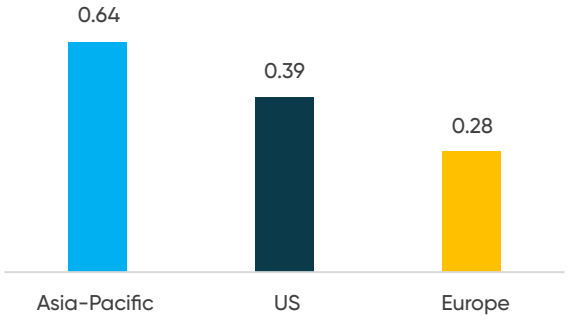


Figure b: Subjects/Site/Month



Source: GlobalData, February 2024

4. REVIEW OF KEY PRECISION ONCOLOGY TRIALS IN 2023

The tables below present a review of recent major advances in precision oncology and the sections that follow will discuss the future implications of these advances, specifying the iterative progress achieved from the end of 2022 through 2023 based on the data from OncoKB. As of November 2023, twelve treatments were approved by the FDA for unique biomarker-selected indications, and six biomarker- and indication-specific treatments were listed in the National Comprehensive Cancer Network (NCCN) guidelines in the past year. Additionally, two precision oncology therapies received level 3 investigational agent status in OncoKB based on compelling clinical evidence (see Table 1). [8]

Table 1: The changes in 2023 precision oncology landscape as documented by OncoKB

Level 1: Biomarkers listed in the tumor type–specific "Indications and Usage" section of the FDA drug label in 2023

Molecular biomarker	Cancer type	Drug	Trial name(s)
ERBB2 amplification	Colorectal cancer	Tucatinib + trastuzumab	MOUNTAINEER
ESR1 oncogenic ligand-binding domain missense mutations (310,547)	Breast cancer	Elacestrant	EMERALD
$BRAF^{V600E}$	Low-grade glioma (pediatric only)	Dabrafenib + trametinib	Study G2201
ATM. ATR CDK12. CHEK2, FANCA, MLH1, MRE11, NBN. PALB2, RAD51C oncogenic mutations	Prostate cancer	Talazoparib + enzalutamide	TALAPRO-2
BRCA1/2 oncogenic mutations	Prostate cancer	Olaparib + abiraterone + prednisone/ prednisolone Niraparib + abiraterone acetate + prednisone	PROpel
FLT3 Internal Tandem Duplication	Acute myeloid leukemia	Quizartinib	QuANTUM- First
Microsatellite instability-high	Endometrial cancer	Dostarlimab + carboplatin + paclitaxel	RUBY
$BRAF^{Y600E}$	Non-small cell lung cancer	Encorafenib + binimetinib	PHAROS
IDH1 R132	Myelodysplastic Syndrome	Ivosidenib	AG120-C-001
ROS1 Fusions	Non-small cell lung cancer	Repotrectinib	TRIDENT-1
PIK3CA. AKT1 or PTEN Oncogenic Mutations	Breast Cancer	Capivasertib + fulvestrant	CAPItello-291

Level 2: Biomarkers listed in the treatment recommendations section of a tumor type–specific NCCN guideline in 2023

Molecular biomarker	Cancer type	Drug	Trial name(s)
$KRAS^{G12C}$	Pancreatic adenocarcinoma	Adagrasib Sotorasib	KRYSTAL-1 CodeBreak 100
ESR1 oncogenic ligand-binding domain in-frame insertions or deletions	Breast cancer	Elacestrant	EMERALD
ERBB2 amplification	Biliary tract cancer	Trastuzumab + pertuzumab	MyPathway
ALK fusions	Inflammatory myofibroblastic tumors	Alectinib	A phase III trial of alectinib vs. crizotinib in pts with ALK+ NSCLC
IDH1 oncogenic mutations	Oligodendroglioma	Ivosidenib	A phase trial of ivosidenib in pts with IDH1 mt glioma
$KRAS^{G12C}$	Colorectal and rectal cancer	(Sotorasib or adagrasib) + (cetuximab or panitumumab)	KRYSTAL-1 Adagrasib or adagrasib + cetuximab CodeBreak 101 Sotorasib + panitumumab

Level 3: Biomarkers predictive of response to targeted agents as demonstrated by phase III clinical evidence, compelling phase I/II trial data in 2023

Molecular biomarker	Cancer type	Drug	Trial name(s)
IDH1R13 and IDH2R172	Oligodendroglioma, astrocytoma	Vorasidenib	INDIGO
FGFR2 oncogenic mutations FGFR2 fusions	Cholangiocarcinoma	(Sotorasib or adagrasib) + (cetuximab or panitumumab)	ReFocus

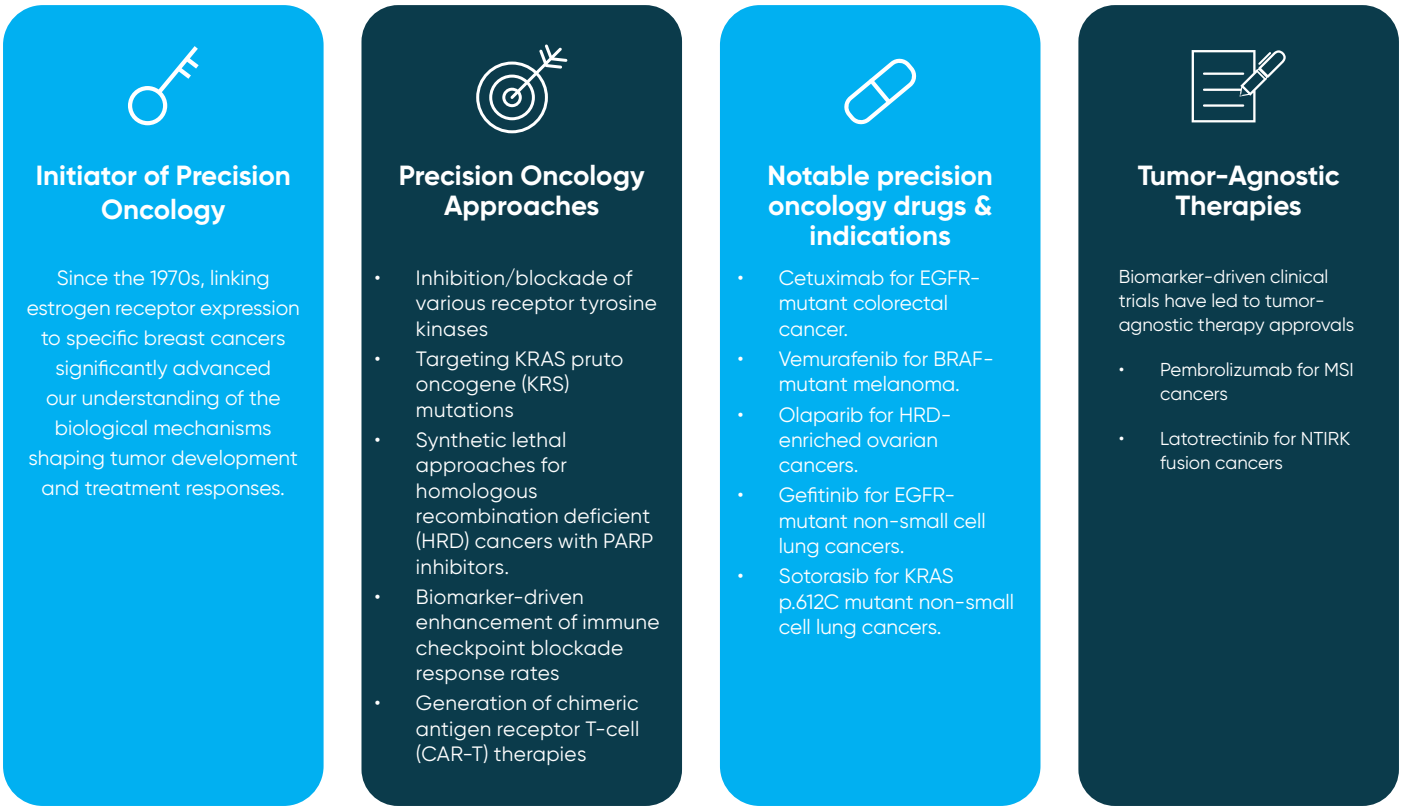
Source: Murciano-Goroff YR, Suehnholz SP, Drilon A, Chakravarty D. Precision Oncology: 2023 in Review. Cancer Discovery. 2023 Dec 12;13(12):2525-31.

5. PRECISION ONCOLOGY MILESTONES: TRACKING TRENDS IN FDA APPROVALS (1998-2023)

Navigating precision oncology: From biological insights to clinical triumphs

Over the past few decades, advancements in comprehending tumor development, especially in breast cancer, has led to diverse mechanisms of action in precision oncology, like inhibiting receptor kinases and targeting mutations. Clinical trials, involving drugs such as cetuximab for colorectal cancer and pembrolizumab for microsatellite instability, showcase targeted therapy successes. Additionally, biomarker-driven strategies have led to the approval of tumor-agnostic therapies like larotrectinib for cancers with NTRK fusions. Precision medicine is now applied in treatment decision-making for several prevalent cancers, including colorectal, breast, lung, certain leukemia and lymphoma types, melanoma, esophageal, stomach, ovarian, and thyroid cancers. The Figure 8 below summarizes various indications for which precision oncology approaches are applied, and the emergence of tumor agnostic therapies. [4,9]

Figure 8: Precision oncology approaches and indications



An investigation on FDA-approved precision oncology therapies and biomarker progress

A recent investigation conducted by Dr. Debyani Chakravarty and her team at Memorial Sloan Kettering Cancer Center (MSK) revealed that close to 83% (164) of the 198 oncology drugs approved by the FDA were categorized as molecularly targeted therapies with known mechanisms of action, and not requiring biomarker testing for patient selection. About 43% (86) of the 198 FDA-approved oncology drugs (1998 to 2022) fall under the category of precision oncology therapies. These therapies, directed by biomarker testing, encompass various types such as kinase inhibitors, small molecule inhibitors, monoclonal antibodies, immune checkpoint inhibitors, and antibody-drug conjugates. Since the initial approval of drugs like trastuzumab (Herceptin) for HER2-positive breast cancer and Imatinib for chronic myeloid leukemia, the pace of FDA approvals for precision oncology witnessed a gradual rise from 1998 to 2017, followed by a significant surge from 2017 to 2022, reaching its peak in 2020.

Among the 86 precision oncology drugs, 80% (69) featured a detectable genomic biomarker through next generation sequencing and proved most effective in tumors with alterations in 45 distinct genes or specific genomic signatures (such as microsatellite-high or tumor mutation burden-high). MSK investigators classified the 69 drugs as 48% (33) first-in-class, 10% (7) with a unique mechanism of action, and 42% (29) as follow-on/resistance precision therapies. The analysis further revealed a significant increase in precision oncology drug approvals since 1998, notably from 2017 to 2022, with a median of 8 annual approvals. During this period, the FDA approved 23 first-in-class drugs targeting 31 novel biomarker-selected patient populations and 18 follow-on drugs, with 2020 alone seeing 12 approvals, including 8 first-in-class and 4 follow-on drugs.

From 2017 to 2022: Tracking progress in actionable biomarkers with MSK-IMPACT®

The eligibility of cancer patients for precision oncology has been a debated topic due to a lack of consensus on actionable gene mutations. To address this, researchers at Memorial Sloan Kettering Cancer Center (MSK) conducted an analysis using the MSK-IMPACT® (Integrated Mutation Profiling of Actionable Cancer Targets) clinical assay (the first laboratory-developed FDA-approved tumor profiling test) on over 47,000 solid tumors, referencing the 2017 and 2022 versions of the OncoKB™ precision oncology knowledge base. The findings, published in Cancer Discovery, demonstrated an increase in the proportion of clinically actionable tumors, defined by the presence of OncoKB™ Level 1 or Level 2 predictive biomarkers of therapy response, rising from 8.9% in 2017 to 31.6% in 2022. It's important to mention that this analysis did not encompass targeted therapies, like chimeric antigen receptor (CAR) T cell therapies and certain antibody-drug conjugates, that do not necessitate molecular testing before initiating treatment. The increase in actionable mutations over the past five years reflects the impact of extensive molecular profiling studies, advancements in clinical trial design (such as cross-tumor basket trials), and reduced costs along with enhanced accuracy in next-generation sequencing-based diagnostic assays, according to Debyani Chakravarty, PhD, a molecular geneticist at MSK and senior author of the study. The findings highlight an ongoing requirement for new precision therapeutics, particularly for cancers with presently undruggable driver mutations. [10,11]

First-in-class drug approvals that drove the significant increase in clinical actionability during 2017 to 2022 include the drugs summarized below: [10]

Table 2: First-in-class drug approvals (2017 to 2022)

Drug Approval	Indication	Percentage Impact on Cancer Type
Alpelisib	PIK3CA-mutant breast cancer	28% of breast cancers
Erdafitinib	FGFR3-mutant bladder cancer	24% of bladder cancers
Pemigatinib, Infigratinib, Futibatinib	FGFR2-fusion-positive cancers	6% of FGFR2-fusion-positive cancers
Ivosidenib	IDH1-mutant cholangiocarcinoma	10% of cholangiocarcinomas
Selpercatinib, Pralsetinib	RET-fusion-positive lung and thyroid cancers	2% and 11% of lung and thyroid cancers, respectively
Sotorasib	The first KRAS G12C-targeted agent for non-small cell lung cancer	Increased Level 1 biomarker predictive of treatment response by 12 percentage points
Agnostic Tumor Type Approvals	Providing options for rare or unknown primary tumors	21.4%(305) of 1,423 patients with cancers of unknown primary eligible, for Level 1 precision oncology drug

At the end of 2023, out of the 217 FDA approved oncology therapies, 94 are precision oncology (43%). Of these, 78 therapies have a biomarker that can be identified by a DNA/NGS-based detection method. Table 3 provides a list of targeted and precision oncology drugs approved in the year 2023. [12] An important trend here is that the range of therapeutic options has expanded to encompass novel drug categories like protein degradation therapies e.g. FDA approved Elacestrant for patients with ER–positive, endocrine therapy–refractory, HER2-negative breast cancer with an ESR1 mutation), and others like bispecific T cell engager (BiTE) therapy, a bispecific antibody, which binds to both an antigen on tumor cells and a surface molecule on T cells, inducing tumor lysis. [8]

Table 3: FDA approved targeted and precision oncology therapies (2023)

Year of drug's first FDA-approval	FDA-approved drug(s) a	FDA drug label listed biomarker(s) b	Class of agent(s) c	Mechanism of action or drug target c	Targeted therapy	Precision oncology therapy	Can a DNA/NGS-based method be used for biomarker detection? d
2023	Capivasertib	PIK3CA, AKT1 or PTEN Oncogenic Mutations and HR+/HER2-	Small molecule kinase inhibitor	AKT1/2/3 inhibitor	Y	Y	Y
2023	Elacestrant	ESR1 Ligand-binding domain missense mutations and ER+/HER2-	Hormone therapy	Selective estrogen receptor degrader (SERD)	Y	Y	Y
2023	Elranatamab		Bispecific T-cell engager	Bispecific BCMA-directed CD3 T-cell engager	Y	N	NA
2023	Enfortumab vedotin + Pembrolizumab		Antibody drug conjugate and immune checkpoint inhibitor combination	Nectin-4-directed antibody and microtubule inhibitor conjugate + Anti-PD-1 antibody	Y	N	NA
2023	Epcoritamab		Bispecific T-cell engager	Bispecific CD20-directed CD3 T-cell engager	Y	N	NA
2023	Fruquintinib		Small molecule kinase inhibitor	VEGFR1/2/3 inhibitor	Y	N	NA
2023	Glofitamab		Monoclonal antibody	CD20-CD3 bispecific antibody	Y	N	NA
2023	Pirtobrutinib		Small molecule kinase inhibitor	BTK inhibitor	Y	N	NA
2023	Quizartinib	FLT3 ITD Mutations	Small molecule inhibitor	FLT3 inhibitor	Y	Y	Y
2023	Repotrectinib	ROS1 Fusions	Small molecule kinase inhibitor	Multi-targeted kinase inhibitor (targets include ROS1 and NTRK1/2/3)	Y	Y	Y
2023	Retifanlimab		Immune checkpoint inhibitor	Anti-PD-1 antibody	Y	N	NA
2023	Talquetamab		Bispecific T-cell engager	Bispecific GPRC5D-directed CD3 T-cell engager	Y	N	NA
2023	Toripalimab		Immune checkpoint inhibitor	Anti PD-1 antibody	Y	N	NA
2023	Eflornithine		Small molecule inhibitor	Ornithine decarboxylase inhibitor	Y	N	NA

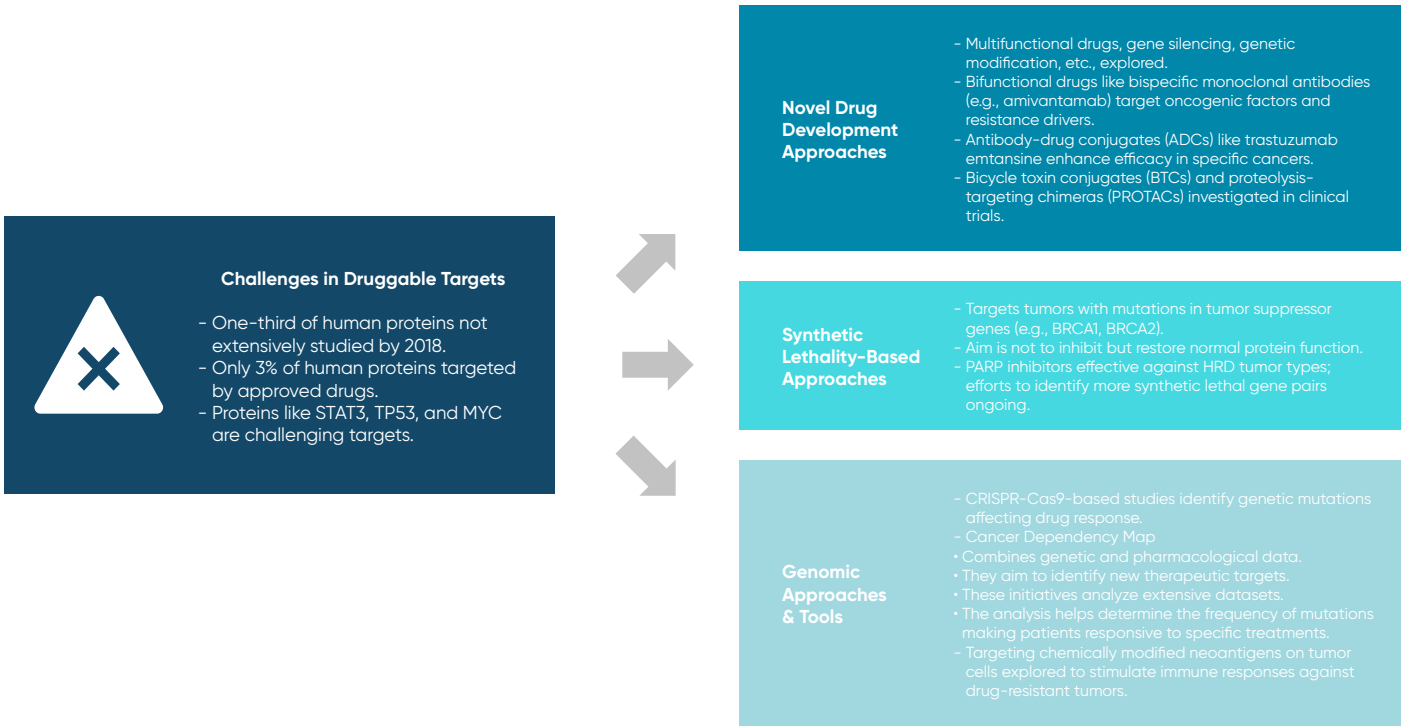
Source: https://www.oncokb.org/oncology-therapies; Suehnholz et al., Cancer Discovery 2023 and Chakravarty et al., JCO PO 2017.

Navigating the druggable landscape: Presenting challenges and pioneering solutions in drug development

In precision oncology, a significant challenge is the limited understanding of potentially druggable targets, with one-third of human proteins unstudied and only 3% targeted by approved drugs. Findings from the Illuminating the Druggable Genome initiative in the US revealed this gap in 2018. While many proteins can be selectively targeted, challenging entities like STAT3, TP53, and MYC remain non-druggable. Overcoming this challenge requires novel drug development approaches, including multifunctional drugs, gene silencing, and synthetic lethality, particularly for cases with oncogenic mutations, treatment resistance, and loss of function as the underlying cause of cancer. Integrating multi-omic data is crucial for identifying new targets and mechanisms of action. This overview (see Figure 9) highlights key points in addressing target limitations, innovative drug development approaches, synthetic lethality, and the role of genomics.

Strategies such as tackling protein complexities, investigating multifunctional drugs, harnessing genomic insights, utilizing gene editing, exploring synthetic lethality, employing advanced genomic tools, and promoting immune stimulation emerge as crucial pathways to advance cancer treatment. These approaches pave the path for the development of more effective and personalized cancer therapies in the future.[9]

Figure 9: Challenges and approaches in precision oncology drug development



6. ONGOING AND UPCOMING DEVELOPMENTS IN PRECISION ONCOLOGY – BEYOND GENOMICS AND EVOLVING TRIAL DESIGNS

Precision oncology progressed over the last two decades through trials like IMPACT (2007), SHIVA (2012), NCI-MPACT (2013), IMPACT II (2014), NCI-MATCH (2015), TAPUR (2016) and DRUP (2016). Recently launched studies like the ComboMATCH, Myelo-MATCH, and iMATCH (see table 4) are further advancing the sector. Developments in molecular technologies and targeted therapeutics have significantly improved precision oncology, leading to better outcomes for specific patients. The use of next-generation sequencing and biomarker assessments refine treatment choices, optimizing patient care. The integration of artificial intelligence, machine learning, and bioinformatics for analysing complex multi-omic data holds promise for more accurate tumor characterization, expediting the implementation of precision medicine. Ongoing trials contribute to improved outcomes and swift identification of curative strategies for cancer patients. [3]

Challenges remain, including the insufficient widespread adoption of molecular testing and advanced technology, along with limited patient access to methods for reversing carcinogenesis and eradicating cancer. Despite these challenges, the last two decades have seen substantial progress, emphasizing the growing effectiveness of precision oncology in treating advanced cancer patients. For example, precision oncology, has boosted pancreatic cancer patient life expectancy by a year through targeted therapies. Additionally, declines are reported in non-small cell lung cancer mortality resulting not just from reduced incidence but also attributed to targeted treatments. Traditional pharmaceutical and healthcare tech companies investing in personalized care, are now beginning to extend precision medicine beyond oncology to areas like immunology, neurodegenerative diseases, and chronic illnesses. Treating each patient uniquely is therefore gaining traction as the standard approach.[13]

Table 4: Recently commenced precision oncology trials

Study Name	Objective & Focus	Key Features
ComboMATCH	Targeted drug combinations for specific cancer gene signatures to address drug resistance in solid tumors.	- Phase II trial - Includes solid tumors like lung, breast, colon, pancreatic cancers - Integrates pediatric patients
MyeloMATCH	Expedite drug development for AML and MDS patients, targeting residual disease as patients progress through different tiers.	- Four-tier study - Five clinical baskets - Phase 2 randomized studies - Emphasis on precision as patients advance
iMATCH	Evaluate immunologic profiles for trial selection; assess response rates based on biomarker subgroups.	- Focus on immune markers - Primary endpoint: objective response rate - Pilot study: combination treatment for advanced cancers

Source: Song, I.-W.; Vo, H.H.; Chen, Y.-S.; Baysal, M.A.; Kahle, M.; Johnson, A.; Tsimberidou, A.M. Precision Oncology: Evolving Clinical Trials across Tumor Types. Cancers 2023, 15, 1967

Beyond genomics: Broadening perspectives in precision medicine through multi-omics and comprehensive patient data integration

Current applications of precision medicine are primarily informed by genomics, which include using tumor genetics to assess risk of developing certain cancers. Genomic biomarkers are also used to determine the appropriate treatment or monitor response. Although there are many uses for genomics yet to be explored, the future of precision medicine will go beyond genomics and consider other characteristics. These characteristics include other omics (transcriptomics (gene expression), proteomics (proteins), lipidomics (cellular lipid pathways and networks) and circulating tumor cells or DNA (ctDNA). Medical, family, and social history, along with environmental

factors and other observable patient data—including lifestyle or behavioral information noted by physicians and gathered through wearables, personal devices, and other methods—are anticipated to inform medical interventions and clinical management. [13]

Adapting clinical trials and infrastructure for precision oncology beyond randomized controlled trials to integrated molecular tumor boards

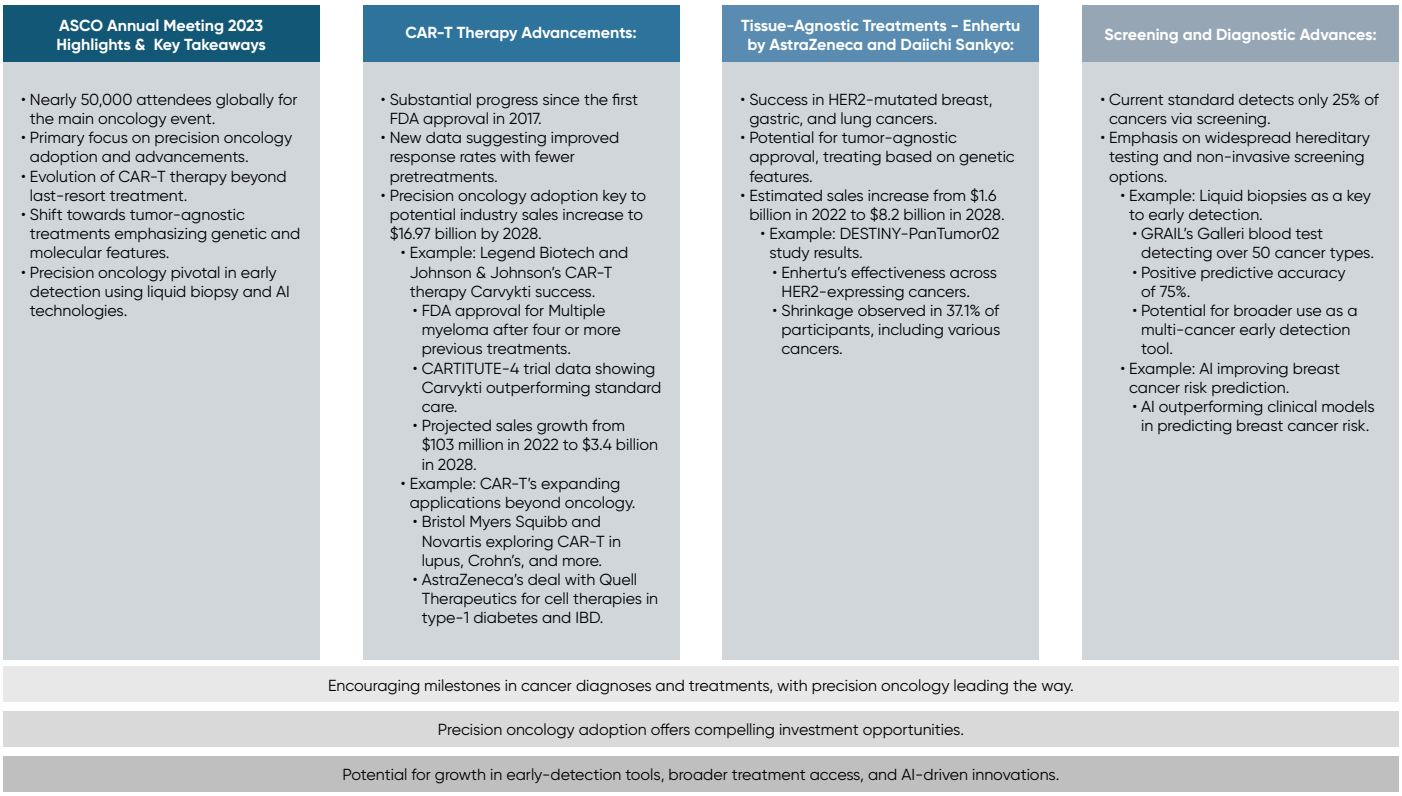
To support the expansion from genomics and beyond, clinical trials for precision oncology are beginning to shift away from the gold standard of randomised controlled trials (RCTs) towards studies that enable broader identification of vulnerable tumours. Precision oncology has advanced significantly due to technology, understanding carcinogenesis mechanisms, and effective anticancer agents. Trials typically involve Next-Generation Sequencing (NGS) and biomarker analyses but vary in sequencing panels and bioinformatics methods. Many institutions have begun implementing infrastructure and decision-support systems such as molecular tumour boards, for integrating genomic analysis with patient data. Certainly, precision medicine stands as a revolutionary advancement in oncology, recognized as one of the most innovative developments in recent medical history. While its potential is vast, ensuring healthcare equity remains crucial to guaranteeing that the benefits of personalized medicine are accessible to all populations across the world. [1]

Cancer screening and diagnostic advances and latest insights from the American Society of Clinical Oncology (ASCO)

By 2023, the FDA approved 155 companion diagnostic devices for targeted drugs across tumor types like breast, lung, and hematologic malignancies, linked to specific molecular aberrations such as BRCA mutations and KRAS G12C. Despite challenges like inconsistent molecular testing adoption and limited patient access, a positive trend has emerged. Implementing AI and bioinformatics enhances accuracy in tumor characterization, promising improved patient outcomes. Ongoing trials like IMPACT/IMPACT2 and NCI-MATCH not only highlight challenges but also signify the increasing momentum and potential of precision oncology, paving the way for more tailored and effective cancer treatments in the coming years.[3]

In 2023, the American Society of Clinical Oncology (ASCO) hosted its 59th Annual Meeting featuring significant developments in precision oncology, with a focus on improving screening and diagnostic methods, increasing patient access to precision oncology, and the widespread adoption of digital health in cancer treatment. Key takeaways included the expanding reach of CAR-T therapy into earlier cancer treatment stages, a potential shift towards tumor-agnostic treatments, and advancements in liquid biopsy and AI technologies for early cancer detection. Key highlights of the meeting are summarised below. (see Figure 10) [14]

Figure 10: Key highlights of the 59th Annual Meeting of ASCO (2023)



Impact of tissue-agnostic drug development - Precision oncology complexities and collaborative solutions for expanded patient outreach

Precision oncology's shift from traditional histology to molecular aberrations, promises personalized cancer treatment but presents challenges in clinical trials. Trials target specific genomic alterations, cutting across various cancer types, creating heterogeneous patient populations, and complicating evidence generation. Regulatory bodies face dilemmas in assessing benefit-risk profiles for histology-agnostic drugs, demanding new frameworks. Pan-cancer trials pose a challenge to statistical models, necessitating a delicate balance between scientific advancement and the need for strong evidence, while also taking patient perspectives into account. Collaborative efforts, such as the Translational Research and Precision Medicine Working Group led by ESMO, are essential in establishing frameworks for histology-agnostic, biomarker-driven trials. This aids in enhancing trial robustness and facilitating streamlined regulatory approval processes. The future of precision oncology hinges on collaborative initiatives, dialogue, adaptive research methodologies and regulatory frameworks. [15]

The growing significance of precision oncology, the rise of novel drug classes, and increasing biomarker complexities are prompting adaptive changes in clinical trial designs. Many therapies now achieve effective target inhibition at doses below the maximum tolerated dose, focusing on long-term tolerability beyond initial toxicity concerns. Recognizing this shift, the FDA initiated Project Optimus in 2023 to refine dose optimization strategies, including patient randomization across various dose levels. To expedite patient access to effective treatments, the FDA permits early introduction of combination therapies, leveraging preclinical data like resensitizing tumors with new inhibitors. Trial designs are also evolving to include earlier-stage interventions, utilizing circulating tumor DNA to identify patients who might benefit from treatments despite lacking radiologic disease signs. Concurrent adjustments in clinical trial designs aiming to optimize dosing strategies and involving patients in earlier disease stages, foster collaboration among precision oncology, molecular oncology, and related fields. These collective efforts thereby offer a broader range of treatment options to a larger patient population. [8]

Biomarker driven clinical trials

The evolving landscape of biomarker-driven clinical trials has been vital in evaluating targeted therapies efficiently and cost-effectively. This innovative approach is crucial for patient stratification and the development of precision oncology. Among the trial designs are basket, umbrella, and platform trials, collectively known as master trials, each contributing distinct methodologies to assess target-agent combinations based on genetic aberrations. The below table (see Table 5) summarizes biomarker driven trial types, with notable trial examples, indications and trial outcomes.

Table 5: Biomarker driven trial types

Trial Type	Description	Notable Example	Key Findings and Results	Indications
Basket Trials	Evaluate one targeted therapy in various cancer types simultaneously, forming a single- or multiple-arm trial. One arm acts as a "basket," allocating small cohorts with a common molecular alteration, investigating the efficacy of one targeted agent. This approach disregards tumor type, histologic features, or patient characteristics, focusing solely on the shared molecular alteration.	NCI-MATCH trial with 24 sub-studies, such as EAY131-H showing efficacy in BRAF V600E mutations.	- Positive results in EAY131-H: Combination of BRAF inhibitor dabrafenib with MEK inhibitor trametinib in BRAF V600E mutations. - Other arms showing activity in AKT-mutated cancers and non-colorectal cancers.	Various solid tumors, including lung, colorectal, breast, and melanoma
Umbrella Trials	Assess multiple targeted therapies in patients with one cancer type but different genetic alterations, conducting sub-studies for each molecular marker. These trials allow for a comprehensive exploration of multiple treatment options within a specific cancer type, tailoring interventions to the unique genetic makeup of individual patients.	National Lung Matrix Trial (NLMT) investigated 8 drugs in 22 molecularly defined cohorts for advanced NSCLC.	Encouraging anti-tumor activity in various signalling pathways, with notable results in ROS1 gene fusion, MET exon 14 skipping, EGFR T790M mutation, RAS activation, and more.	Non-Small Cell Lung Cancer (NSCLC)
Platform Trials	Clinical trials with an open master protocol, allowing multiple treatments to enter or exit based on observed results throughout the study. These trials employ adaptive designs to swiftly respond to emerging data, fostering a dynamic exploration of targeted therapies in various cancer settings.	I-SPY 2, an ongoing platform trial investigating neoadjuvant treatments in patients with locally advanced breast cancer.	- Graduation of agents to phase III, including HER-2 receptor inhibitor neratinib and PARP inhibitor veliparib. - Positive impact of pembrolizumab in triple-negative and hormone receptor-positive, HER2-negative breast cancer.	Locally advanced breast cancer
Hybrid Trial Designs	Overlapping trial types, combining elements of basket and umbrella trials. For example, the TAPUR study assesses off-label use of FDA-approved targeted therapies in patients with actionable genomic variants. These hybrid trials offer flexibility, exploring both approved and investigational drugs for specific genomic variants across different cancer types.	TAPUR study showing promising activity in various cancers.	Positive results in NSCLC, breast, and colorectal cancer sub-studies, demonstrating anti-tumor activity for drugs such as palbociclib, pembrolizumab, and capivasertib.	Various solid tumors, including lung, breast, colorectal

The surge in biomarker-driven clinical trials, depicted by basket, umbrella, and platform trials, highlights a paradigm shift towards personalized medicine in oncology. The precision medicine approach, guided by reliable biomarkers and supported by faster tracks to clinical implementation, not only enhances treatment efficacy but also minimizes toxicity. These advancements reveal a promising future in the quest to combat and potentially cure cancer through tailored therapeutic strategies, with several agents potentially attaining FDA approvals based on their positive outcomes in master trials. [43]

7. PRECISION ONCOLOGY - FUNDING INITIATIVES ACROSS THE GLOBE

Government and public-private partnerships

Global funding drive precision oncology advancements, and supporti initiatives like the US Government's Cancer Moonshot with a $94 million allocation for VA programs and $215 million for the VA Medical Care program. In Europe, PCM4EU (EUR 3 million) and PRIME-ROSE (EUR 6 million) revolutionize cancer care. In Asia-Pacific, LC-SCRUM-AP promotes genome medicine for lung cancer, while the Australian Precision Medicine Enterprise (APME) Project secured a $23 million Federal grant, marking a significant stride in advancing precision medicines. These initiatives collectively shape the future of cancer care, emphasizing precision oncology's pivotal role in the global fight against cancer. (see Table 6)

Table 6: Government and public-private funding initiatives

Name of the Initiative by Location	Description

U.S. Government Initiatives - PMI and Cancer Moonshot [16,17]	• **Precision Medicine Initiative® (PMI)**
	  • Launched in 2016
	  • Received $215 million investment from President Obama's 2016 Budget
	  • Aim: Expedite biomedical research and equip clinicians for personalized therapy
	  • $70 million dedicated to the National Cancer Institute (NCI)
	  • Focus on advancing precision oncology
	• **Cancer Moonshot**
	  • Launched in 2016
	  • 2024 budget allocation: $94 million for VA research programs
	  • $215 million for the VA Medical Care program
	  • Focus on precision oncology for optimal cancer care for veterans
	  • Funding also supports research on rare cancers, cancers in women, genetic counselling, tele-oncology, and precision oncology programs

Precision Oncology Ireland [18]	• Collaborative initiative for precise cancer diagnoses and treatments • Brings together academic institutions, industry partners, and charitable organizations • Coordinated by Systems Biology Ireland • Part-funded by the Strategic Partnership Programme of Science Foundation Ireland (SFI) • Consortium involves universities: University College Dublin, Trinity College Dublin, Royal College of Surgeons in Ireland, University College Cork and NUI Galway • Industry partners include AstraZeneca, Celgene Institute for Translational Research Europe, Cell Stress Discoveries, Genuity Science, Helsinn Group, pHion Therapeutics and OncoMark • Charities involved: Breast Cancer Ireland, Breakthrough Cancer Research, Irish Cancer Society, National Breast Cancer Institute, National Children's Research Centre and The Oesophageal Cancer Research Fund • Collaborative effort commenced in 2019 • Aim: Advance precision oncology research and implementation • Combined funding commitment of €11.9 million over five years
The European Partnership for Personalised Medicine (EP PerMed) [19]	• Backed by a €375 million budget from the EU • Supported by over 50 global partners • Aims to enhance future healthcare in the region • Focus areas: personalized therapy, diagnosis, and prevention • 10-year objective: Advance transnational development and translation of personalized medicine • Acts as a global platform for scientific dialogue • Accelerates implementation steps • Promotes demonstration projects • Goal: Showcase evidence of personalized medicine implementation • Contribution to improved health outcomes within sustainable healthcare systems
Drew Foundation Precision Oncology Center of Excellence [20]	• Initiated in 2021 by the Prostate Cancer Foundation (PCF) - a leading philanthropic organization, founded in 1993 by Mike Milken • Allocated $2.5 million for the launch • Collaboration with the University of California, San Francisco (UCSF), and the San Francisco VA Health Care System (SFVAHCS) • Dedicated to providing state-of-the-art precision oncology treatments • Exclusive focus on Veterans dealing with prostate cancer • Ensures all Veterans have access to breakthrough medical treatments • Precision medicine is integral, incorporating gene sequencing • Customizes treatments based on individual biological and genetic characteristics • Extends PCF's network to 13 Centers of Excellence nationwide • Advances precision oncology treatments and research for Veterans • Contributions to studies on various cancers, including COVID-19 support

Name of the Initiative by Location	Description
	• Dedicated to funding groundbreaking research for prostate cancer with over $860 million raised • Supports over 2,200 research projects across 220 cancer centers in 22 countries worldwide.
European Investment Bank Funding for ITM [21]	• ITM Isotopen Technologien München AG secured €40 million in funding from EIB in 2020 • Specializes in the development, production, and global supply of advanced diagnostic and therapeutic radiopharmaceuticals for precision oncology • Funds earmarked for research and development investment • Proprietary portfolios focus on targeted radionuclide diagnostics and therapies • Specifically designed for addressing various cancers, including neuroendocrine tumors and bone metastases.
AstraZeneca Canada and Illumina - Collaboration with Breast Cancer Canada [22]	• Breast Cancer Canada (BCC), in partnership with AstraZeneca Canada and Illumina, introduced a $200,000 research grant (2023) • Aimed to support Canadian research teams utilizing precision diagnostics and AI for advancing breast cancer screening and detection • Illumina contributes in-kind donations of sequencing consumables for collaboration facilitation • Initiative focuses on identifying researchers using innovative precision or personalized technologies, including blood tests, imaging, and machine learning • BCC unveils the 2024 Annual Breast Cancer Research Grants, allocating a significant $500,000 in fresh Canadian funding • Demonstrates commitment to advancing impactful research for new discoveries and improved care amidst evolving trends in breast cancer research and funding
Advancing Precision Oncology in Canada - Genomic Initiatives and Accessible Healthcare Solutions [23,24]	• Diverse initiatives with a $255 million investment in fifteen projects launched by Genome Canada, the Canadian Institute of Health Research, and other partners • Initiatives span various medical areas since 2012, aiming to make precision medicine more accessible • Addressing gaps in genomic understanding among Indigenous populations is a key focus • British Columbia residents can obtain DNA tests at pharmacies for personalized cancer pharmaceutical recommendations • Active investment in genomics infrastructure, exemplified by the Genomics Cloud, fostering collaboration and data sharing • Terry Fox Research Institute launches a 'precision medicine' network, uniting researchers, and healthcare professionals across Canada • Federal government commits $150 million over five years to support collaborative efforts, involving researchers from institutions such as Memorial University • Demonstrates Canada's commitment to advancing precision oncology for a diverse population.
Genomics Thailand Initiative - $150 Million Investment [25]	• Genomics Thailand Initiative - recently approved for a substantial $150 million investment over five years • Aims to characterize the genomes of 50,000 citizens, and contributes to the establishment of a local genetic data bank relevant to the local and Asian populations • The bank serves as a valuable reference for genetic normality • Differs from databases primarily derived from Western populations
Singapore's National Precision Medicine Strategy - Genetic Data Banks Expansion [26]	• Implemented to expand genetic data banks for diverse health insights • Involves the collection of genetic material from 10,000 healthy individuals, across diverse ethnicities • Progressed to the second phase in 2021 • Plans to expand the data bank to include 100,000 healthy individuals • Aligns with the broader integration of precision medicine into clinical practices • PRECISE (Precision Health Research, Singapore) spearheads the initiative • Government-wide effort with a 10-year National Precision Medicine strategy • The third phase scheduled to commence in 2024
China's Precision Medicine Initiative - $9.2 Billion Strategy [25]	• A $9.2 Billion Strategy Transforming Healthcare • Played a pivotal role in acquiring and accessing data for millions of individuals, particularly focusing on oncology • Prioritized precision medicine during the 13th Five-Year Plan (2016-2020) • Allocated substantial funding of $9.2 billion for PMI by 2030 • Largest and most well-funded precision medicine initiative globally • Presents lucrative opportunities for domestic and international players • Aims to strengthen their presence in the Chinese and Asian markets

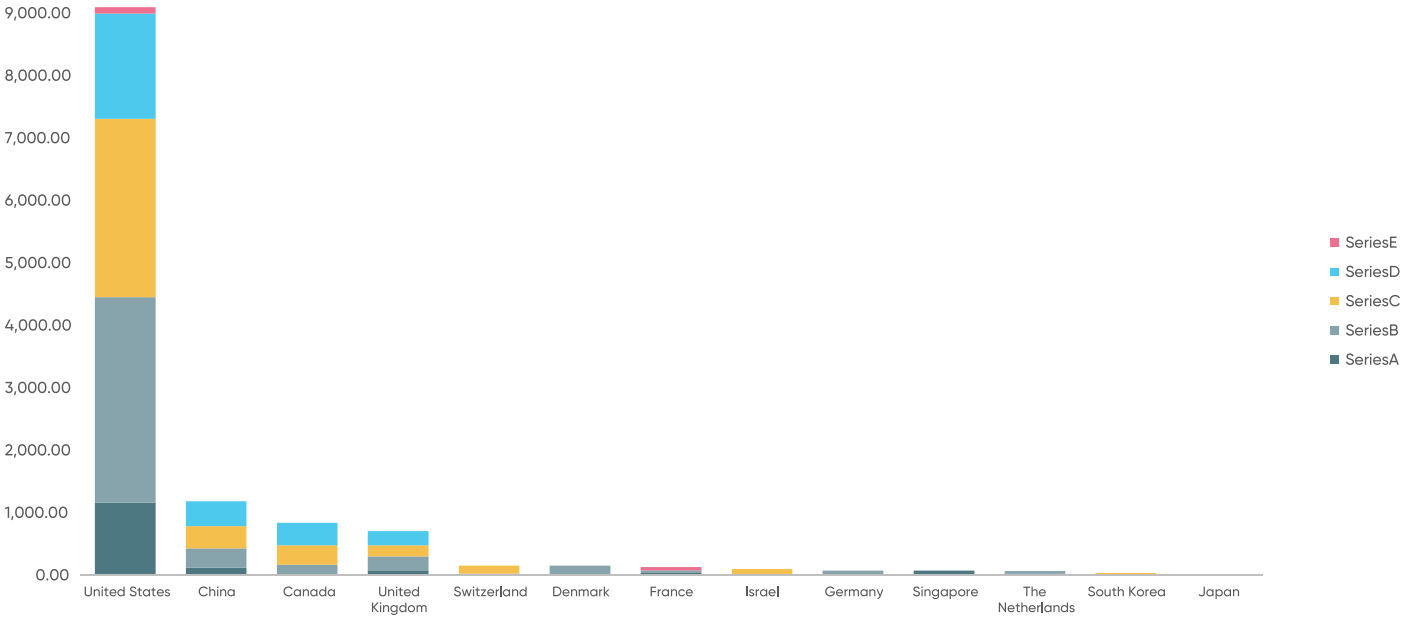
Name of the Initiative by Location	Description
K-MASTER Project - Genomic Insights in Korea [27,28]	• Initiated in Korea in June 2017, and led by Korea University as a clinical trial platform • Utilizes NGS assays to screen actionable mutations in 10,000 patients with refractory solid tumors • Aims to analyse genomic data from over 5,000 cancer patients and conducts clinical trials based on the genomic data • Aligns clinical trials with each patient based on genomic analysis results and aims to achieve optimal precision medicine outcomes • Receives a five-year, 70 million funding commitment from the South Korean government • Focuses on genomic sequencing, clinical trials, and the development of a cancer genomics database in precision oncology • Collaborates globally with organizations like the American Association for Cancer Research and the Dana-Farber Cancer Institute • Shares genomic profiling data to advance diagnostic technologies and treatments
LC-SCRUM-AP - Lung Cancer Genomic Screening [29,30]	• A lung cancer genomic screening initiative involving 20 medical institutions in the Asia-Pacific region • PREMIA (Precision Medicine Asia Co., Ltd), in collaboration with NCCHE (National Cancer Center Hospital East), launched LC-SCRUM-AP • Aims to advance precision medicine development in the Asia-Pacific region; countries include Thailand, Malaysia, Vietnam, Singapore, Indonesia, Australia, and Taiwan • Expanded across the entire Asia-Pacific region to facilitate international drug development and to advance lung cancer research, and contributes to the development of therapies for driver gene-positive lung cancer • LC-SCRUM-Asia, underway in Japan • Registers over 18,000 lung cancer patients • Creates a large clinico-genomic database through LC-SCRUM-AP and fosters academic partnerships across the Asia-Pacific • Japanese medical insurance covers lung cancer genomic screening, including single gene and NGS panels (AmoyDx PLC PCR Panel is a reimbursed companion diagnostic) • Taiwan and Southeast Asia lag in supportive health insurance, hindering precision medicine accessibility – hence Japan's success offers a model for Asia-Pacific countries to expedite health insurance inclusion and enhance accessibility
Australian Precision Medicine Enterprise (APME) Project's $23M Federal Grant for Precision Medicine [31]	• The APME Project - a collaboration between Global Medical Solutions Australia (GMSA), Telix Pharmaceuticals, and Monash University • Secured a $23 million Federal government grant in 2022. • Grant Program: Manufacturing Collaboration Stream of the Modern Manufacturing Initiative (MMI) • Aim: Revolutionize large-scale development and manufacturing of precision medicines and theranostics • Geographic Focus: Australian and Asia Pacific markets • Funding Commitment Over Three Years: $41.2 million (GMSA Contribution: $25 million; Telix Pharmaceuticals Contribution: $5 million; Monash University Contribution: $11.2 million) • Telix Pharmaceuticals - Specializes in clinical-stage products for oncology and rare diseases • Monash University - A leading research-intensive institution providing cutting-edge research platforms, and which facilitates technology transfer and contributes to economic impact in Victoria

Precision Cancer Medicine Across Europe - Initiatives and Collaborations [32]	• **PCM4EU (Personalised Cancer Medicine for all EU citizens)**
	  • Funding Source: EU4Health programme with a budget of EUR 3 million
	  • Objective: Implement molecular cancer diagnostics for precision oncology in the EU
	  • Geographic Focus: Coordination across 15 European countries
	• **PRIME-ROSE (Precision Cancer Medicine Repurposing System Using Pragmatic Clinical Trials)**
	  • Funding Source: Horizon Europe Programme with a budget of EUR 6 million
	  • Objective: Unite seven clinical trials across Europe
	  • Focus Areas: Data gathering, standards and advancing precision cancer medicine
	• **MATRIX (Norwegian Centre for Clinical Cancer Research)**
	  • Funding Sources: The Norwegian Cancer Society and the Norwegian Research Council, with a budget of NOK 128 million
	  • Objectives: Extend lives, Improve cancer care, Focus on innovative diagnostics and Adopt patient-centered approaches
	  • Geographic Focus: Norway

Venture funding landscape

From 2019 to 2023, disruptive technology companies engaged in precision oncology consistently saw the United States taking the lead in venture funding, securing substantial investments (approximately $9,000 million) across all funding series, from Series A through Series E. Although just receiving one ninth of the funding received by the top player, China emerged second ($1,185 m), playing a key role, and receiving considerable funding from Series A through Series D. Canada and the United Kingdom are other top countries which secured significant investments, particularly Canada for Series B ($170.83 million), Series C ($312.00 million), and Series D ($360.00 million); the UK for Series B ($224.00 million), Series C ($180.00 million), and Series D ($225.00 million). Switzerland secured funding primarily for Series C ($129.00 million). Denmark, France, Israel, Germany, Singapore, the Netherlands, South Korea, and Japan each played a role in precision oncology funding, contributing to the global effort in advancing cancer treatment strategies. This breakdown highlights the diverse global landscape of precision oncology funding, reflecting a collaborative effort to drive innovation and advancements in cancer treatment strategies across various countries. (see Figure 11)

Figure 11: Funding (US$m) in precision oncology by top locations (2019-2023)



Source: GlobalData, January 2024

In precision oncology venture funding by series (2019-2023), Series B and Series C dominate with a combined investment of $8,376.19 million, reflecting a focus on mid-stage development. Series D follows with $2,752.97 million, while Series A and Series E exhibit comparatively lower funding at $1,544.70 million and $157.25 million, respectively. The concentration on mid-stage financing suggests a prioritization on maturing technologies and clinical advancements. (see Figure 12)

In precision oncology venture funding by year (2019 to 2023), the trend reveals a remarkable surge from 2019 to 2021, reaching a peak of $4,729.47 million. However, there is a significant drop in 2022 to $1,443.33 million, followed by a further decline in 2023 to $701.30 million. Factors such as regulatory changes and increased scrutiny may have impacted investor confidence, affecting precision oncology venture funding. In addition, global economic conditions and uncertainties may have influenced overall healthcare sector investment trends. Furthermore, technological hurdles and competition for funding among startups may have hindered precision oncology projects, affecting investor interest. Most importantly, the lingering effects of the COVID-19 pandemic could have disrupted operations, clinical trials, and research activities, impacting the overall funding landscape. (see Figure 13)

Figure 12: Sum of deal value (US$m) by series

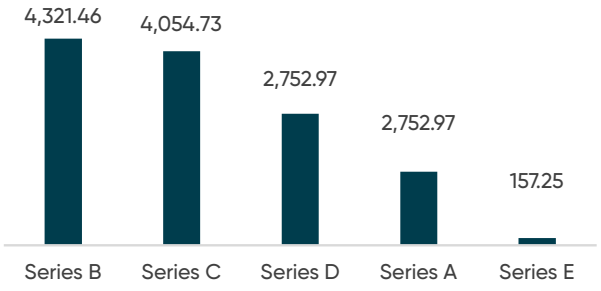
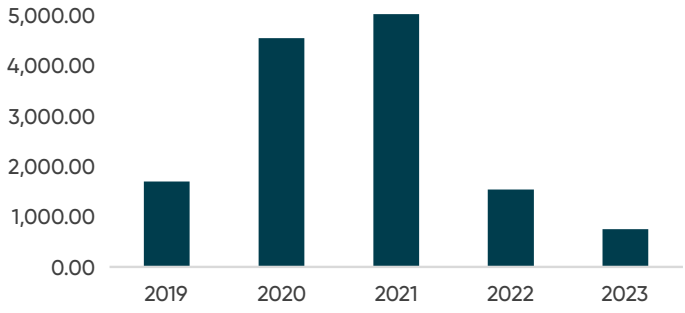


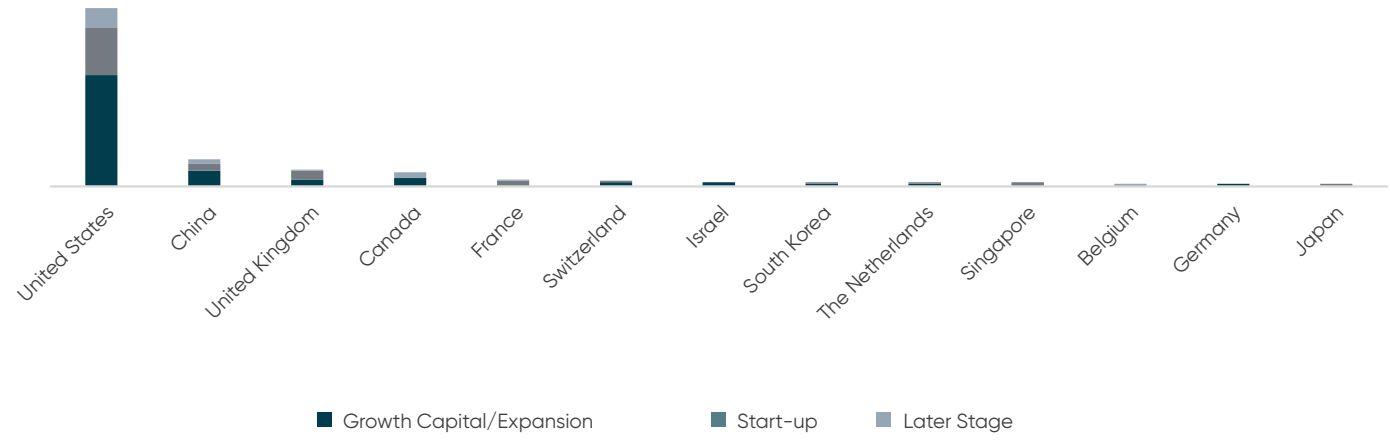
Figure 13: Deal value (US$m) by year



Source: GlobalData, January 2024

Precision oncology venture funding deals (2019 and 2023) by locations and by stage of development saw the United States as the leading hub, accounting for a sizable 125 deals across different developmental stages, solidifying its position as a key player in the industry. China followed with 19 deals, indicating the nation's increasing significance in the precision oncology space. The United Kingdom, Canada, and France rounded out the top five, each contributing significantly with 12, 10, and 5 deals, respectively. The deals spanned various stages, encompassing Growth Capital/ Expansion, Start-up, and Later Stage, highlighting the broad spectrum of development phases within the precision oncology sector across these key locations. The higher number of deals in Growth Capital/Expansion suggests a strategic focus on scaling successful ventures that have demonstrated promise and potential. Simultaneously, the presence of Start-up and Later Stage deals highlights the sustained interest and investment across different developmental stages, indicating a comprehensive approach to supporting innovation and advancement in precision oncology. (see Figure 14). The top companies which received venture funding in the range from 200 US$m to 400 US$m include XtalPi Inc, Kriya Therapeutics Inc, InSilico Medicine, Recursion Pharmaceuticals Inc, Kallyope Inc, Affinivax Inc, Arbor Biotechnologies Inc and Erasca Inc.

Figure 14: # Deals by stage of development across locations



Source: GlobalData, January 2024

8. KEY TRENDS IMPACTING PRECISION ONCOLOGY RESEARCH AND DEVELOPMENT

Outlined below are the primary trends that will shape the landscape of precision medicine in the next two years. These are categorized into four domains: healthcare, technology, regulatory and macroeconomic trends.

Healthcare Technology Regulatory Macroeconomic

Cell, Gene therapies & RNA-based therapies

- Gene therapy, including CRISPR technology, is revolutionizing precision medicine with over 4,450 drugs in trials. Encompassing vectors, therapeutic oligonucleotides, genome editing, and oncolytic viruses, this category offers new treatment paradigms, with expected sales reaching $54 billion by 2029. High development costs are a hurdle; AI and IoT integration may cut costs. Novel reimbursement strategies aim to enhance patient access to gene therapies. Examples include Alnylam's Amvuttra (RNAi), Novartis's Leqvio (RNAi) and Sarepta's Elevidys (gene therapy)
- Cell therapy market set to generate $52 billion by 2029, with gene-modified therapies like Carvykti leading. Autologous challenges addressed with rapid manufacturing advances. Rising investment in allogeneic (off-the-shelf) therapies for wider patient access. Gamida Cell's Omisirge, the first allogeneic stem cell therapy, approved in 2023.
- mRNA-based vaccines (e.g., for COVID-19) drive interest. Antisense oligonucleotides and mRNA cancer vaccines show promise as personalized medicine, with over 1,200 drugs in the pipeline.

Genomic advancements

- From Human Genome Project to rapid, affordable sequencing, genomics fuels personalized medicine.
- DTC genetic tests (e.g., 23andMe) empower patients, but ethical concerns persist.

Diagnostic Biomarkers

- Biomarkers drive swift drug discovery for personalized treatments.
- Advanced diagnostic tools (genomic, proteomic, imaging) enhance early detection and monitoring.
- Liquid biopsies, like ctDNA monitoring, gain traction.
- Unmet needs include a demand for more predictive biomarkers.
- Foundation Medicine's molecular profiling
- There are people who have a significant number. There are people who have a significant number of followers in every business.

Digital health technologies

- IoT in healthcare collects real-world data, enabling remote monitoring and generating digital biomarkers.
- Wearable technologies track vital signs, offering preventative and predictive insights.
- Electronic Health Records (EHRs) integrate diverse patient data, supporting precision medicine decisions.

Big data and AI

- Healthcare and pharma leverage big data for precision medicine. CertisAI platform by Certis Oncology Solutions, launched in April 2023, uses big data and machine learning to study predictive biomarkers for improved oncology drug development.
- Advances in machine learning, like OpenAI's GPT-3, drive AI applications in drug discovery, clinical trials, and patient recruitment. Ocean Genomics uses AI to identify predictive variants in mRNA. Companies like Akkure Genomics, Deep6 AI, and MatchMiner use AI for patient recruitment.

Digital Twins

- Digital twins simulate patients or biological processes for personalized medicine.
- Quinten Health optimizes clinical trials, while Alcaris Theranostics models tumor responses.
- Challenges include environmental impact, human body complexity, and privacy issues.

Cloud Computing

- Cloud computing accelerates precision medicine by digitizing health data.
- Qiagen migrates to the cloud for effective diagnostic software.
- Supports decentralized clinical trials, overcoming challenges in patient recruitment.

Nanotechnology

- Nanopharmaceuticals, combining drugs with nanocarriers, offer opportunities in cancer treatment.
- Companies like Novartis and Clarity Pharmaceuticals explore theranostics, integrating diagnosis and treatment.

Robotics & 3D Printing

- Robotics revolutionizes the pharma value chain, from drug discovery to manufacturing. Multiply Labs collaborates for automated gene-modified cell therapy manufacturing. Takeda invests in a robotics-enabled cell therapy factory.
- Anticipated uses of 3D printing in healthcare include personalized drug printing and bioprinting of human cells and tissues.Bioprinted stem cells enable personalized disease treatment. 3D-printed drugs tailored to patient characteristics could transform the market.

Regulation of Personalized and Precision Medicines

Drug regulation encompasses various aspects, and precision medicines face unique challenges due to their targeted nature.

Regulatory agencies update rules, allowing the use of real-world evidence (RWE) for approval.

FDA's progress includes guidance on gene therapy and CAR-T cell therapy, and the creation of the regenerative medicine advanced therapy (RMAT) designation.

Reimbursement Landscape

- Drug reimbursement poses a major challenge for precision medicine adoption.
- Complexities include drug shortage concerns, ESG pressures, and lack of alignment in reimbursement processes. Innovative payment models, like installment payments, emerge.
- Policies demand proof of clinical benefits and long-term cost reduction.

Regulation of Diagnostic Tools Supporting Precision Medicine

- The regulatory environment for diagnostic tools supporting precision medicine is uncertain.
- Inconsistent regulation, especially for laboratory-developed tests, creates challenges.
- Regulatory bodies globally are re-evaluating approaches.
- CDx regulations streamline co-development processes, aligning pharmaceutical and medical device organizations.

Data Privacy Concerns

- Tougher rules imposed on protecting patient data due to concerns of insufficient action by companies.
- GDPR in the EU and HIPAA in the US ensure data privacy.
- Stricter regulations essential for handling personal health data required for precision medicine.
- Pseudonymization balances data protection and supporting real-world evidence.
- Differing global data privacy rules may lead to data-sharing silos, slowing precision medicine development.

Drug Prices, Market Entry, and Economic Inflation

- Drug pricing challenges persist due to high development costs, affecting precision medicine adoption.
- Regulatory changes in Germany and the US (Inflation Reduction Act) impact pharmaceutical pricing.
- Merck & Co challenges the US government.
- CSL Behring's Hemgenix, priced at $3.5 million per dose, exemplifies cost concerns.

Industry Activity – Mergers & Acquisitions

- M&A activity rebounded in 2023, showcasing pharma companies' confidence in precision medicine.
- Pfizer's $43 billion acquisition of Seagen and Merck & Co's $10 billion acquisition of Prometheus Biosciences contributed to the resurgence.
- Big pharma builds precision portfolios through acquisitions.

Demographic Changes

- Global aging populations increase the prevalence of chronic diseases
- Precision medicine addresses unmet needs in cancer and neurodegenerative diseases such as Alzheimer's. E.g. Brainvectis's BVCYP-01 gene therapy targets Alzheimer's pathology.
- Aging populations require more efficacious drugs and preventative care, driving precision medicine opportunities.

China Seeking to Capture Market Share from the United States

- Both the US and China heavily invest in precision medicine R&D. The US leads in commercialization, with established companies like Merck & Co and Pfizer.
- China invests $9 billion in a 15-year Precision Medicine Initiative to challenge the US pharmaceutical market.
- The initiative focuses on establishing China as a leader, developing genetic sequencing technologies, and leveraging its large population for AI models.
- Although China lags in development, ongoing investments and integration of AI in big data analytics could reshape the industry.
- China's regulatory efforts focus on building a robust precision medicine industry, with ongoing investments and initiatives to streamline drug approvals.

Strategic partnerships

- Strategic partnerships are crucial for advancing accessible precision medicines.
- Collaborations drive drug development, prove efficacy, and overcome commercialization challenges.
- Partnership activity peaked in 2020 but declined in 2022.
- Key partners of co-development partnerships include Kite Pharma, AstraZeneca, and Bluebird Bio.

Global Precision Medicine Landscape:

- US dominates precision medicine trials and has more approved drugs.
- China is rapidly growing its presence, especially in cell and gene therapies.
- Global competition for precision medicine leadership is evident, with precision oncology driving the surge in targeted therapies.
- Leading CAR-T cell therapies like Kymriah and Yescarta lead in the US.
- China focuses on developing and testing oncology precision medicines contributing to the global landscape..

Source: GlobalData, 2023

9. SWOT ANALYSIS AND GLOBAL INITIATIVES FOR EQUITABLE ACCESS OF PRECISION ONCOLOGY THERAPIES

SWOT analysis

Precision oncology, a dynamic field at the intersection of healthcare and technology, exhibits a distinctive set of strengths, weaknesses, opportunities, and threats (SWOT). As advancements continue to reshape the landscape of cancer care, understanding these internal and external factors becomes paramount for strategic decision-making. Here's a concise overview of the SWOT analysis for precision oncology:

INTERNAL FACTORS	
STRENGTHS (+)	**WEAKNESSES (-)**
1. Personalized Treatment: Tailored strategies based on individual molecular and genetic profiles enhance treatment outcomes.	**1. Cost and Accessibility:** High costs of genetic testing and therapies may limit accessibility, creating disparities among socioeconomic groups.
2. Targeted Therapies: Precision oncology enables therapies directed at specific genetic mutations, improving precision and reducing side effects.	**2. Incomplete Molecular Understanding:** Gaps in understanding some cancers' molecular intricacies limit precision oncology effectiveness.
3. Advancements in Technology: Technologies like NGS and CRISPR/Cas allow comprehensive molecular profiling and identification of therapeutic targets.	**3. Complexity:** Precision medicine involves intricate processes, including genetic testing and interpretation
4. Research and Government Support: Government investments, like the Canadian government's $255 million funding, contribute to ongoing precision oncology advancements.	**4. Data Integration Challenges:** Managing large-scale patient data, integrating diverse sources, and ensuring data security pose significant challenges.
	5. Reimbursement Issues: The lack of adequate reimbursement models for precision medicine hinders its widespread adoption.
	6. Educational Gaps: Healthcare professionals need more training and awareness about precision oncology implementation.

EXTERNAL FACTORS	
OPPORTUNITIES (+)	**THREATS (-)**
1. Drug Development and Innovation: Ongoing research and technological advancements create opportunities for innovative drugs and therapeutic approaches.	**1. Ethical and Privacy Concerns:** Use of genetic information raises ethical concerns, emphasizing the need for robust regulatory frameworks.
2. Evolving Clinical Trial Designs: Evolving clinical trial models (basket, umbrella, and platform trials) enhance drug development efficiency. Adaptive methodologies, patient-centric approaches, and advanced technologies streamline biomarker identification, fostering personalized interventions and optimizing combination therapy exploration in precision oncology	**2. Resistance and Adaptation in Tumors:** Tumor cells developing resistance to targeted therapies require ongoing research to overcome such mechanisms.
3. In-Silico Modelling: Advances in disease modelling through in-silico, in-vitro, and in-vivo methods offer unprecedented opportunities for drug discovery and personalized treatment.	**3. Regulatory Hurdles:** Stringent regulations and approval processes impact the adoption of novel precision therapies.
4. Emerging Markets: Expanding into untapped markets can drive adoption and accessibility of precision oncology.	**4. Lack of Expertise:** The shortage of skilled professionals proficient in precision medicine implementation.
5. Predictive Biomarkers: Increasing use of predictive biomarkers for cancer diagnostics opens new avenues for targeted therapies.	
6. Collaboration and Data Sharing: Increased collaboration and data sharing accelerate discoveries and enhance precision oncology effectiveness.	

While precision oncology medications offer significant potential, they encounter obstacles associated with data, reimbursement, and expertise. Successfully navigating the complex domain of precision oncology requires harnessing strengths, rectifying weaknesses, seizing opportunities, and countering threats. This is vital for propelling patient-centric care forward and ushering a transformative era in cancer treatment. [33,34,35,36,37]

Bridging gaps: A global initiative for wider and equitable access to precision oncology therapies

In precision oncology, ensuring widespread access to innovative therapies is paramount. Tailoring recommendations to address limitations in essential including medicine lists, diagnostic capabilities, and affordability. These strategic actions are designed to propel progress in precision oncology, fostering international collaboration, strengthening infrastructure, and advancing equitable healthcare access across the world. The strategic actions needed to maximize global access of novel precision oncology therapies are summarized below. [38]

Figure 15: Bridging gaps for equitable access to precision oncology therapies

Limited WEM List

- Regularly update the WHO Model List of Essential Medicines (WEM) to include effective emerging therapies.
- Collaborate with oncologists and health economists to prioritize drugs based on clinical effectiveness, cost-efficiency, and patient requirements.

Limited Diagnostic Capabilities

- Invest in training programs to expand the workforce skilled in PCR-based assays, NGS, WGS and other advanced diagnostics.
- Provide grants and resources for LMICs to adopt and scale alternative diagnostic methods where PCR is impractical.

Accessibility in LMICs

- Strengthen the supply chain infrastructure, leveraging technology for better tracking and distribution.
- Foster public-private partnerships to enhance the availability of essential treatments in both sectors

Lack of Expertise & Infrastructure in LMICs

- Launch a hospital twinning program, connecting institutions in LMICs with those in HICs for mentorship and knowledge transfer.
- Create fellowship exchange initiatives, encouraging HIC oncologists to spend time in LMICs, fostering expertise and collaboration.

High Treatment Costs

- Streamline regulatory approval for biosimilars and generics to promote competitive pricing.
- Create a global consortium for negotiating drug prices with pharmaceutical companies. The MAX Foundation's program, for instance, collaborates globally to provide cost-effective therapies for chronic myelogenous leukemia (CML) while strengthening health systems in LMICs through global physician networks

Affordability & Equity

- Establish academic and nonprofit consortia for researching and advocating equitable drug pricing in LMICs.
- Launch multi-institutional partnerships integrating diagnostics, therapeutics, and monitoring for a comprehensive care model.

10. CONCLUSION

The future of precision oncology: A paradigm shift in cancer treatment

In 2001, the landscape of cancer treatment underwent a significant transformation with the advent of precision oncology. This marked a departure from traditional methods like chemotherapy, radiation, and surgery to a more targeted approach. While small molecules, constituting approximately 60% of FDA-approved drugs, have left a notable impact, their limitations are evident, benefitting only a modest 7%-8% of all cancer patients. Recent breakthroughs, exemplified by drugs like lorlatinib and osimertinib in specific NSCLC cases, hint at progress. However, to bridge the gap between the surge in new drugs and limited patient advantages, continuous enhancements in molecular design are imperative.

The evolving landscape, powered by advanced technologies, instils hope for more precise therapies, especially for historically underserved populations. Although challenges persist in targeting specific elements, an integrated approach is amplifying drug profiles and expanding therapeutic possibilities. This fosters optimism for an era of improved cancer treatments.

Precision oncology stands to revolutionize cancer treatment paradigms, with targeted therapies emerging as the cornerstone of future approaches. Advances in comprehending molecular pathways, coupled with the efficiency of Next-Generation Sequencing (NGS), signal a promising era for personalized cancer care. A vision that involves standardizing genetic tests across diverse cancer types and customizing interventions based on individual tumor characteristics is gaining prominence.

As research advances, the integration of cutting-edge technologies, such as CRISPR/Cas, and the exploration of synthetic lethality extend the capacity to identify therapeutic targets. CRISPR/Cas facilitates precise gene editing, allowing the creation of animal models that mimic patient mutational statuses. This, combined with insights from clinical trials and real-world databases, holds the potential to unlock a broader reach for precision oncology.

Precision oncology fundamentally rejects the one-size-fits-all treatment model, while considering tailored approaches based on each patient's unique molecular characteristics. The future envisions a scenario where a patient's genetic profile becomes a guiding influence on oncology care globally, transforming cancer treatment into a more effective and individualized practice. [39,40,41]

11. APPENDIX

Impact of precision oncology in the near and far term on a selection of cancers

Cancer Type	Near-Term Positive Impacts of Precision Oncology	Far-Term Positive Impacts of Precision Oncology	Impact Level
Breast Cancer	Targeted therapies (HER2, hormone receptor); personalized treatments based on genetic profiling.	Advancements in immunotherapies; precision medicine for rare subtypes; preventive strategies.	
Non-Small Cell Lung Cancer (NSCLC)	EGFR and ALK inhibitors showing efficacy; immunotherapies improving outcomes.	Further subtyping and targeted therapies; enhanced immunotherapies based on molecular insights.	
Chronic Myeloid Leukemia (CML)	Tyrosine kinase inhibitors achieving long-term remission.	Continued development of targeted therapies; deeper molecular understanding for tailored treatments.	
Acute Lymphoblastic Leukemia (ALL)	Targeted therapies and CAR-T cell treatments showing positive outcomes.	Refinement of targeted therapies; broader application of immunotherapies.	
Chronic Lymphocytic Leukemia (CLL)	Positive outcomes with BTK inhibitors and BCL-2 inhibitors.	Further precision in therapeutic interventions; personalized treatment strategies.	
Melanoma	BRAF inhibitors and immunotherapies demonstrating positive impact.	Enhanced targeted therapies; improved immunotherapeutic strategies.	
Ovarian Cancer	PARP inhibitors demonstrating efficacy in BRCA-mutated cases.	Expanded use of PARP inhibitors; exploration of novel targeted therapies.	
Prostate Cancer	Positive impact with androgen receptor-targeted therapies.	Advancements in personalized treatments; refined targeting strategies.	
Gastrointestinal Stromal Tumor	Tyrosine kinase inhibitors (imatinib) showing significant positive impact.	Improved targeted therapies; precision medicine based on individual tumor profiles.	
Colorectal Cancer	Targeted therapies for specific mutations; improved outcomes with immunotherapies.	Subtyping refinements; personalized approaches based on molecular characteristics.	
Acute Myeloid Leukemia (AML)	Emerging targeted therapies improving outcomes; potential for personalized treatment strategies.	Continued advancements in targeted therapies; deepening understanding of AML subtypes.	
Liver Cancer	Developing targeted therapies for specific molecular alterations; improved treatment strategies.	Advancements in liver cancer precision medicine; expanded targeted options.	

Medium High

Emerging start-ups and their innovations in precision medicine [42]

Startup	Key Focus / Description
US-based startup Kinnate Biopharma	- Advancing genomically-defined cancer therapy through selective small molecules targeting genetic mutations and fusions. - Focus on kinases, high selectivity, and broad genetic alteration coverage. - Pipeline includes compounds like Exarafenib Monotherapy and Exarafenib Combination for BRAF, NRAS-driven cancers, and FGFR2/3 gene alterations in solid tumors.
Indian startup OneCell Diagnostics	- Developing dynamic data analytics for precision oncology using the iCore Platform. - AI-enabled biomarker discovery tool automating primary and secondary analysis, fostering collaboration in translational research. - Emphasis on liquid biopsy, NGS diagnostics, and cancer recurrence prediction tools for more precise and personalized cancer management.
Canadian startup Epigene Labs	- Creating an augmented intelligence-based platform for precision oncology research and drug advancement. - mCUBE platform expedites data-driven drug discovery, biomarker identification, and patient selection using AI algorithms. - Integrating publicly available data and proprietary data from partners.
Canadian startup Genomadix	- Creating a Molecular Analyzer for decentralized diagnostics, providing rapid and accurate results without requiring a lab. - The Genomadix Cube, a mobile-based DNA analyzer, uses PCR tests for various applications, including COVID-19, legionella, CYP2C19 mutations, and Alzheimer's disease.
Israeli startup AID Genomics	- Developing genomic and genetic diagnostic products, including early colorectal cancer screening tests based on DNA methylation detection. - Offering a non-invasive prenatal screening tool, NIFTY, with high accuracy for detecting common trisomies and other genetic anomalies. - Providing software solutions like AIDTES for qPCR analysis automation.
US-based startup Imagene AI	- Specializing in AI-based Molecular Profiling for real-time biomarker profiling. - Technology profiles biomarkers directly from biopsy images, eliminating the need for additional tissue samples. - Focusing on non-small cell lung cancer (NSCLC) biomarker profiling and addressing issues associated with traditional diagnostic processes.
US-based startup Ocean Genomics	- Creating an Intelligent Transcriptome Platform for RNA-based innovation in precision medicine. - TxomeAI and DiscoverAI computing platforms integrate transcriptomics with other data sources for drug target and biomarker discovery. - Utilizing the company's vast transcriptome database, DeepSea, for real-time biomarker profiling enabling enhanced diagnostics, therapeutics, for better patient treatment and outcomes.
French startup Predicting Med	- Offering a Pancreatic Cancer Decision Support Platform through its molecular test, Pancreas View. - Providing both prognosis and theranostic insights for pancreatic cancers, aiding oncologists in decision-making. - Emphasizing treatments based on individual genotypes for precise and effective care.
UK-based startup Mantara Health	- Testing Drug-Gene Interaction with the Mantara PGx DNA Test, understanding the effect of metabolized medications. - Analyzing an individual's DNA to determine potential drug-gene interactions, highlighting medications of concern based on genetic makeup. - Assisting healthcare professionals in tailoring prescriptions for safer and more effective treatments.
Indian startup Jeniquen Lifesciences	- Delivering Pharmacogenomics Reporting through GeniqueCARE, translating DNA-based insights for clinicians and patients. - Providing insight into the body's reaction to medication, predicting drug efficacy, and identifying potential adverse reactions based on genetic composition. - Investigating genetic markers across various medical domains for personalized medication.

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