Insight Brief

Navigating the Complex Oncology Landscape

New strategies for clinical trial success

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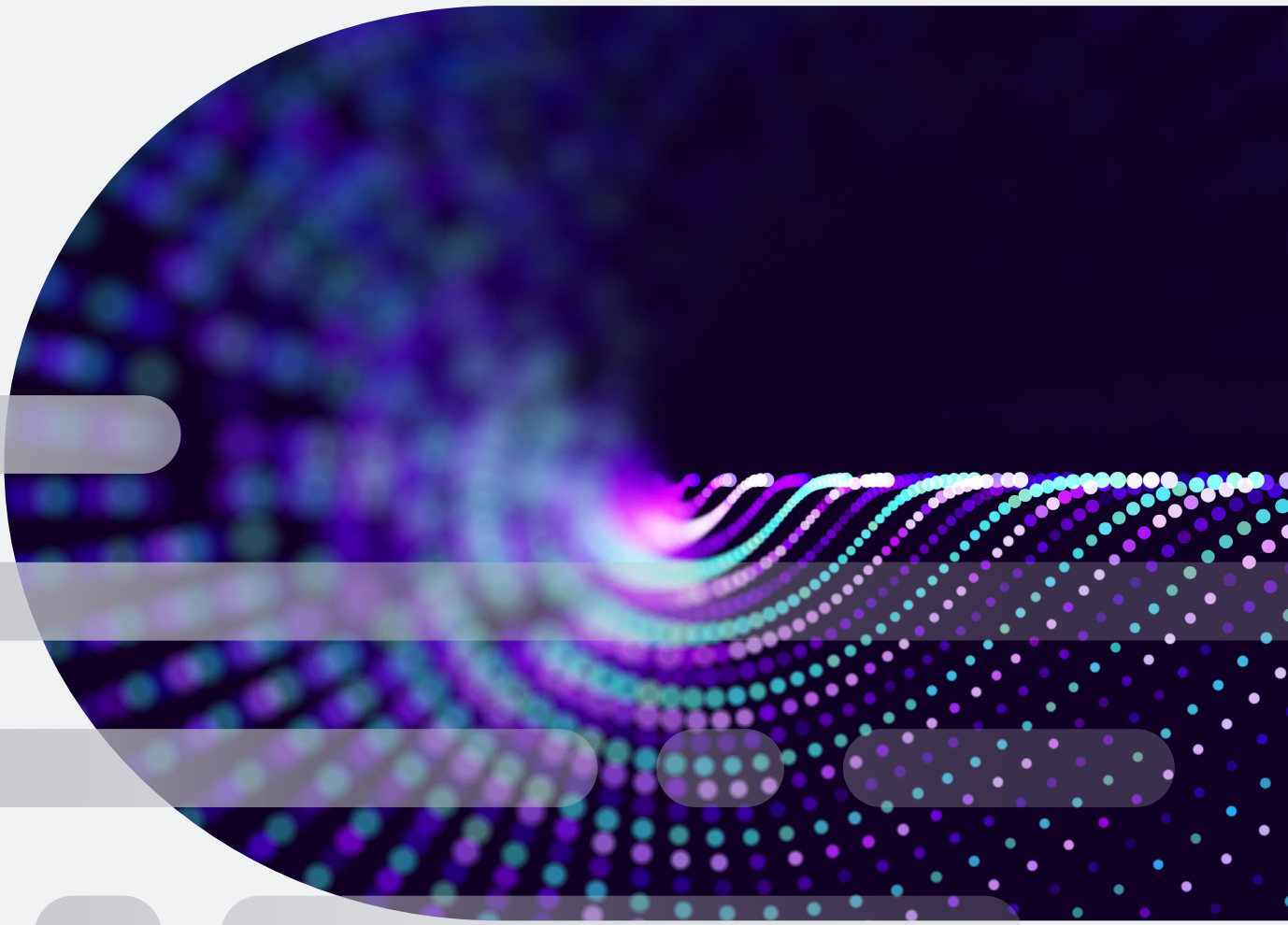


Introduction

Oncology research and development has undergone significant advancements in recent years, with innovative treatment options now offering renewed hope to patients worldwide. This progress is largely driven by emerging biotech companies, which contribute a remarkable 70% of the R&D pipeline. However, these companies face immense challenges, as they are tasked with not only developing groundbreaking therapies but also securing investment funding to sustain their research efforts.

This insight brief draws from the Global Oncology Trends 2023 report by the IQVIA Institute for Human Data Science, and explores the latest oncology trends that affect sponsors and offers guidance for optimizing clinical trial strategy. We take a close look at early phase oncology trial design and strategy, as well as design considerations for platform trials that can broaden access to new treatment options. Finally, we examine efforts made to improve racial and ethnic representation in clinical trials and provide recommendations for building diversity planning into clinical trial protocols.

2023 GLOBAL ONCOLOGY TRENDS

Murray Aitken shares insights from the 2023 Global Oncology Trends report significant to biotech sponsors

Oncology trials have seen a surge in activity levels. In 2022, approximately 2,300 new trials were launched, marking a 30% increase since 2017. Despite brief setbacks and disruptions due to the COVID-19 pandemic, there has been a notable rebound. By 2022, growth had stabilized, but the total number of trials initiated within that year set new records.

The development pipeline has undergone a transformation, attributed to the increase in next-generation biotherapeutics. Antibody-drug conjugates (ADCs) and bispecific antibodies have been garnering interest, especially in the treatment of solid tumors.

Since 2020, immuno-oncologics have maintained a steady presence in cancer treatment approaches, with cell therapies, CAR-Ts, RNA therapeutics, vaccines, gene editing, and gene therapy, gaining traction.

Emerging biopharma and biotech companies, defined as those with an annual R&D expenditure of less than $200 million and earnings under $1 billion, have also played a critical role in industry activity. In fact, these companies are responsible for the active development of 1,600 molecules in 2022 alone; a substantial leap from 400 a decade ago.

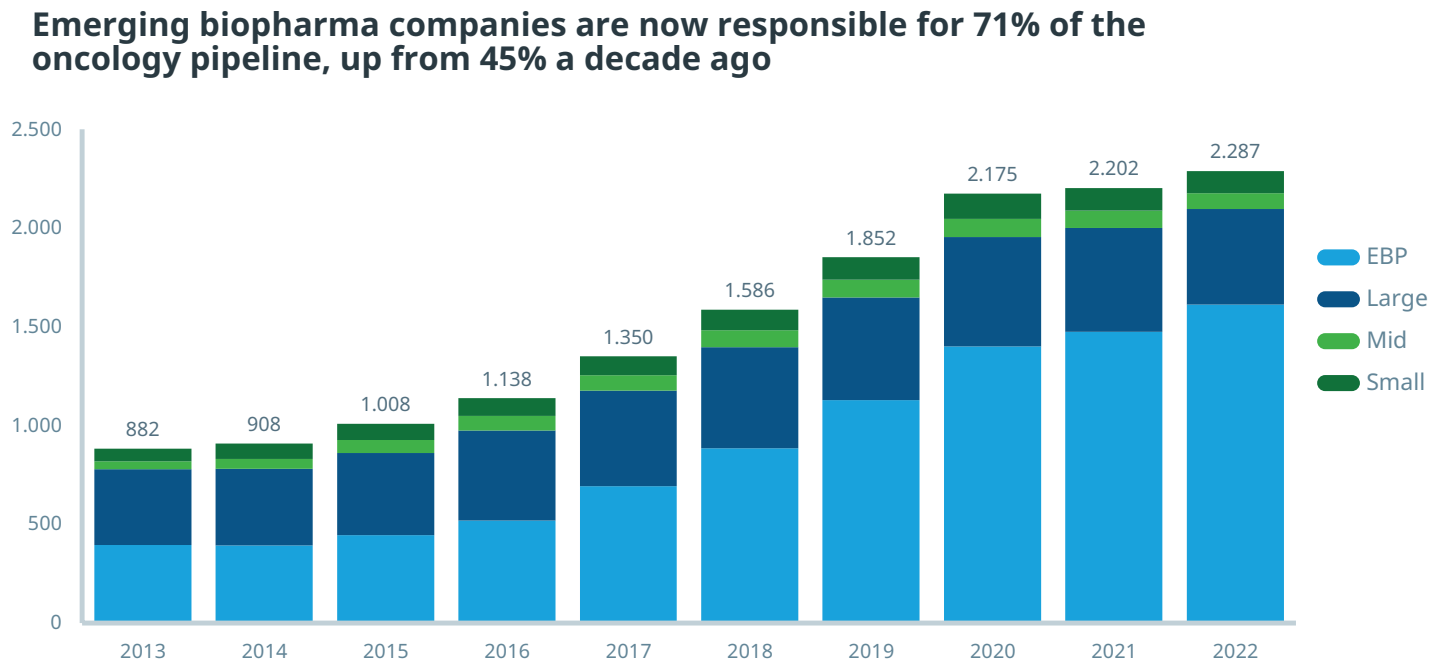


Figure 1. Number of Phase I to regulatory submission oncology pipeline products by company segment, 2013-2022. Credit: IQVIA Institute Oncology Trends 2023 report.

Geographical factors have also influenced the development of molecules by emerging biopharma and biotech companies. China-headquartered companies have had a surge in contributions, rising to 30% of the global pipeline of oncology drugs in development from 13% five years ago. On the other hand, companies headquartered in the U.S. and Europe have seen a decrease in their share, even as the absolute number of molecules in development has increased.

The contribution of emerging biopharma companies is evident not just in the development of drug pipelines, but also in regulatory approval submissions and market launches. In 2022, these companies were responsible for introducing 7 of the 10 launched substances, demonstrating their growing contribution.

The geographic distribution of EBPs with oncology drugs in development has shifted dramatically in the past five years

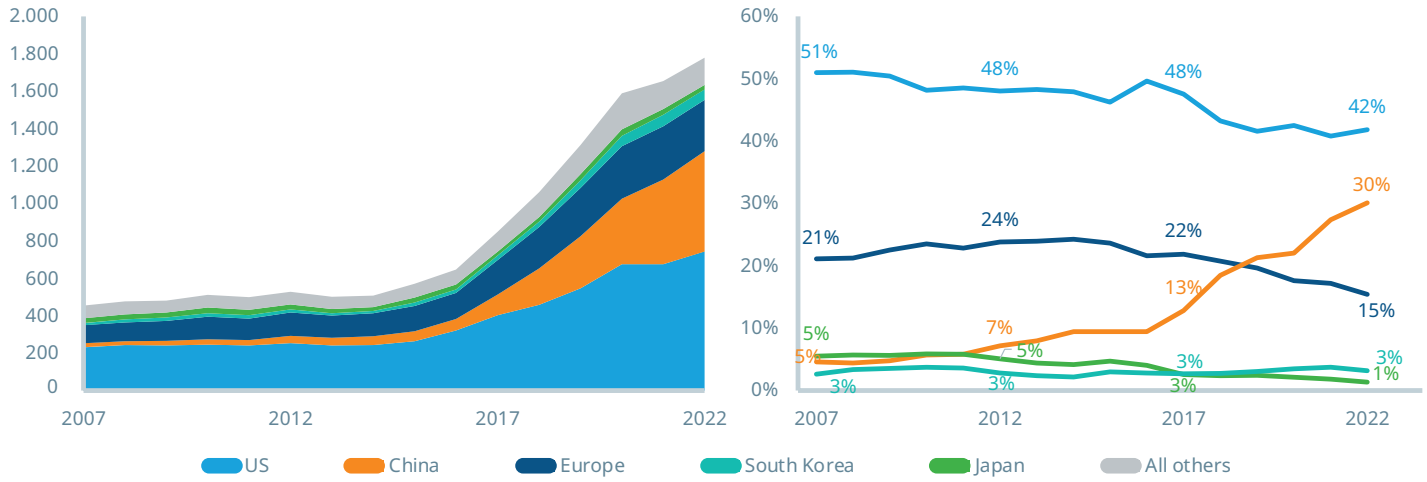


Figure 2. Number of emerging biopharma oncology drugs over time and country share of pipeline Phase I to regulatory submission based on company headquarters location, 2007-2022. Credit: IQVIA Institute Oncology Trends 2023 report.

Undeniably, the last decade has seen a shift in the biopharma landscape. In the past, larger corporations were primarily responsible for marketing drugs developed by emerging biopharmas; however, in recent years, more than half of such drugs have been launched by biopharma organizations themselves.

This trend suggests smaller companies are retaining their assets, guiding them through regulatory submissions and market launches.

CHALLENGES IN ONCOLOGY CLINICAL DEVELOPMENT

The expanding role of biotech companies in advancing therapeutics from development to regulatory submission is a positive change, but they face persistent challenges in oncology clinical development, along with recent initiatives that introduce new stressors and uncertainties:

Success rates

From 2016 to 2022, success rates in oncology clinical development have shown a downward trend across both rare and non-rare, solid, and heme/oncology categories. This trend likely represents companies taking on greater scientific risk in their clinical programs, driven by an increased appetite for breakthroughs from both regulatory and patient outcome perspectives. However, this increased scientific risk also leads to a higher risk of failure, especially in Phase II and beyond.

Complex trials

Oncology trials pose a challenge due to their complexity, which often surpasses other therapy areas. This complexity is reflected in the study duration, participant count, site and country numbers, eligibility criteria, and endpoints. Despite a spike in non-oncology trial subjects due to COVID-19 innovation, oncology remains more intricate.

Trend lines have shown variations, with fewer eligibility criteria, stable endpoint numbers, and reduced site and country numbers, particularly during the pandemic.

The timeline from initial patent filing to U.S. market launch shows more molecules launching within five years, though the overall numbers remain small. This suggests that while rapid development in oncology is possible, most molecules take six to ten years. There's a strong focus on reducing timelines, with the goal to launch more molecules within ten years from the original patent filing. While this has been achieved, it remains an ambitious target.

Financial challenges

While 2020 and 2021 saw exceptional funding levels of $135 billion and $118 billion respectively for the biopharma sector including oncology, in 2022 and 2023-to-date levels are back in line with the long-term trend. This surge followed by a decline to more normal levels brings uncertainty to the sector and remains a challenge for biopharma.

Policy and regulatory challenges

Recent policy and regulatory changes are impacting the pharmaceutical sector. The Inflation Reduction Act in the U.S. has raised concerns about its effects on the industry, especially with Medicare now able to negotiate prices. Additionally, new legislation requires diversity action plans to be submitted to the FDA before pivotal trials begin.

In Europe, a new pharmaceutical strategy is stirring up interest with its major initiatives and potential reforms, but it still needs further action for full enactment.

Other developments include the initiation of joint clinical assessments for Health Technology Assessments in Europe, the FDA's launch of Project Optimus, and increased scrutiny on accelerated approvals by the FDA, suggesting a possible need for rebalancing in this area.

HOW TO OPTIMIZE CLINICAL TRIAL STRATEGY

Gerhard du Toit shares an operational perspective on the trends above as they relate to challenges impacting the industry and increasing complexity of trials.

Operationally, there's been an increased focus on complex novel trial designs and in recent years, over a quarter of industry-backed quality trials have incorporated such designs, notably master protocols.

The industry supports these innovations in clinical trial design and delivery because it can help expedite drug development. This aids pharmaceutical and biotech firms, as well as stakeholders like patient advocacy groups.

LEVERAGING MASTER PROTOCOLS: A STRATEGY FOR STREAMLINING COMPLEX CLINICAL PROGRAMS

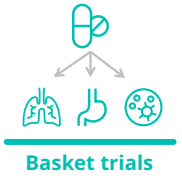
Master protocols are pivotal in executing and streamlining intricate clinical programs. They aid in minimizing development risks by facilitating earlier go/no-go decisions, reducing cycle times and costs for quicker study activation, and distributing infrastructure expenses across multiple arms or sub-protocols.

This strategy also promotes innovation and ongoing learning, enabling efficient research of rare or complex indications and producing real world data.

The design frameworks of master protocols can be tailored to align with a program's objectives, optimizing clinical development. This customization emphasizes the need to understand the unique differences between basket, umbrella, and platform trials:

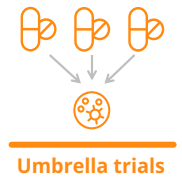
Basket trials

Basket trials involve a single drug targeting multiple areas. These can range from basic solid dose escalation studies to complex Phase I basket studies in multiple cell malignancies, which utilize sub-study expansions, efficiency cohorts, and real world data to cater to this population. This design also allows for the incorporation of different elements within a specific trial.



Umbrella trials

Umbrella trials test multiple agents against the same tumor type, allowing for shared standard care for control patients. These can be used by a single pharmaceutical or biotech company to test a group of agents or a single target, defined either at the indication level or with precision medicine.



Platform trials

Platform trials build on umbrella studies' benefits and often include adaptive design elements. This is achieved through collaboration among biotech firms, patient advocacy groups, and nonprofits to develop and invest in underserved therapies by cost and risk sharing.

Platform designs can accelerate development and improve understanding of patient populations through signal finding and registrational studies. The success of a master protocol requires defining study operations and infrastructure, along with the ability to adjust to dynamic needs, especially when multiple arms of a study are at different stages. This process necessitates strategic planning, flexibility, and quality controls throughout execution.

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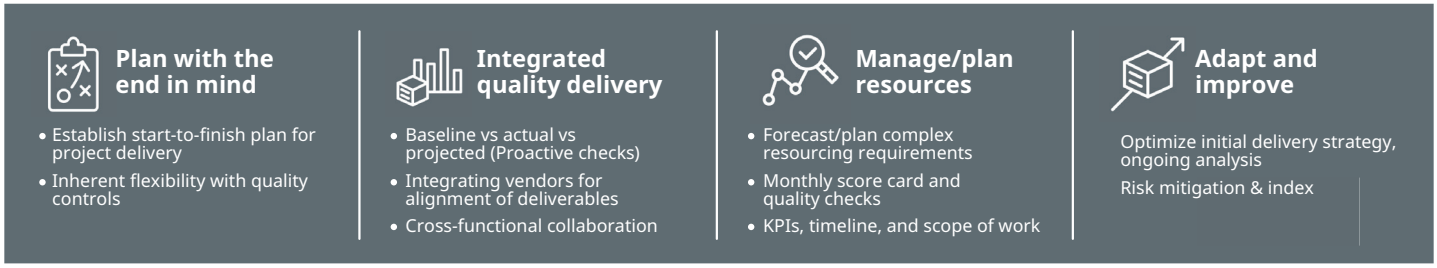
KEY FACTORS TO ENSURE THE SUCCESSFUL OUTCOME OF A MASTER PLATFORM

There are several factors to ensure the successful outcome of a master platform across the full study lifecycle.



EXECUTING IN THE EARLY PHASE ONCOLOGY LANDSCAPE

Having flexible and adaptive trial designs in early phase oncology studies allows the review of emerging safety, PK, and PD data which can result in safer, more informed decision-making, lowering risks and improving overall subject safety with simplicity. Yet, there are specific challenges sponsors must be aware of when executing early phase oncology trials.

Clinical trial saturation, characterized by an increase in trials and fewer recruitment opportunities per protocol, is one crucial factor to consider when executing early phase oncology trials. Post-pandemic staffing constraints in the healthcare sector have resulted in fewer, potentially less experienced personnel. As a countermeasure, the economic environment is pushing for more experienced staff.

Challenges also stem from economic and financial pressures. Investors have become more stringent, demanding higher returns for lower investments. The pandemic's low return on investment has led to a need to compensate.

In addition, the evolving regulatory landscape, including the FDA's Project Optimus draft guidelines, has resulted in delays and trial cancellations. This necessitates a focus on population pharmacokinetics, broad population enrollment, dosage evaluations for subpopulations, and appropriate food effect assessments for oral treatments. Safety considerations call for careful enrollment criteria, initial dosing, real-time data evaluation, and dose modifications.

MEETING THE FIT-FOR-PURPOSE NEEDS OF EARLY PHASE ONCOLOGY STUDIES

To meet fit-for-purpose needs of early phase oncology studies, sponsors should consider three main criteria:

- **Country/Site selection:** Utilizing robust data for strategic planning of optimal country and sites is crucial. Early engagement can lead to a smart selection of sites that can help achieve first patient enrolled (FPI) as well as overall enrollment.
- **Start-up:** Keeping the big picture in mind is important. Establish FPI guidelines and consider conducting a site kick-off meeting to map out start-up plans. Effective communication with sites during start-up and employing technology to ease the burden of document review and delivery are key.
- **Data excellence and decision making:** Implementing a well-defined cohort management plan with tech-enabled communication allows for transparency with sites. In addition, a proactive data cleaning strategy with clear expectations across the clinical, data management and site can help increase trial efficiency, speed and safety.

At IQVIA Biotech, we consider these criteria and focus on enrollment criteria, initial dosage, and real-time data analysis. Our strategic analyses target optimal therapy populations, expected efficacy, patient access, and market needs. We're increasingly utilizing AI in planning and execution stages, including early engagement with PIs and KOL networks. This feeds into strategic planning, involving submission strategies for the U.S. and Europe, and future development country selection and submissions.
In addition, our involvement in Project Optimus review is comprehensive, helping sponsors select a suitable dose-finding strategy and address population evaluation within regulatory constraints.

Biotech sponsors need expertise for early phase studies, requiring flexibility, proactivity, and substantial data investment. Effective monitoring strategies, remote monitoring, and real-time data reporting readouts are essential. The influence of all actions on the study's outcome is understood through an AI system and expert consultation, ensuring accurate submission planning. Building the right team and vendor selection are vital.

DIVERSITY AND INCLUSION FOR CLINICAL TRIALS

Shifting focus to another important consideration, the issue of diversity and inclusion in clinical trials is garnering attention, particularly in the U.S., and is becoming a focal point for regulators and stakeholders.

Over time, the FDA has introduced evolving guidelines, leading to legislative changes requiring a diversity action plan. This plan, submitted before a new drug's pivotal study, must include the sponsor's enrollment goals for each clinical trial, the reasons for these goals, and how they plan to achieve them.

We believe everyone involved in clinical trials, from sponsors to CROs and investigator sites, has a responsibility to increase access for historically underserved populations. This includes understanding and addressing barriers, scrutinizing inclusion/exclusion criteria, and evaluating site selection.

At IQVIA, we have a division that focuses on inclusion/diversity to make sure our approach considers patient and systemic barriers, and we can take the right steps to bring about change.

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SOCIETY, GOVERNMENT, PUBLIC-PRIVATE EFFORTS	SPONSORS, CROS, RESEARCH INSTITUTIONS	SPONSORS, CROS, RESEARCH INSTITUTIONS AND COMMUNITY GROUPS
Improve overall trial awareness and participation	Raise awareness, prioritization among trial operations management and field staff	Involve community groups in outreach, trial education
Increase health literacy among diverse populations	Upskill and support research-naïve sites with intended population	Create culturally sensitive Informed consent material
Reduce disparities in access to health care	Increase pool of diverse, community-based investigators	

A LIFECYCLE APPROACH TO ACHIEVING CLINICAL TRIAL DIVERSITY

Adopting a lifecycle approach to achieving diversity in clinical trials begins with careful consideration of trial design and site selection. It continues through site activation and supports the communication expectations associated with patient recruitment, culminating in data retention. Revisiting trial design from the outset, including goal setting and site selection, is integral to this process. It not only complements the master protocol but also focuses on staff involvement, site activation, and diversity-centered patient recruitment. All these elements are designed to ensure continuous patient and site engagement and feed into data retention.

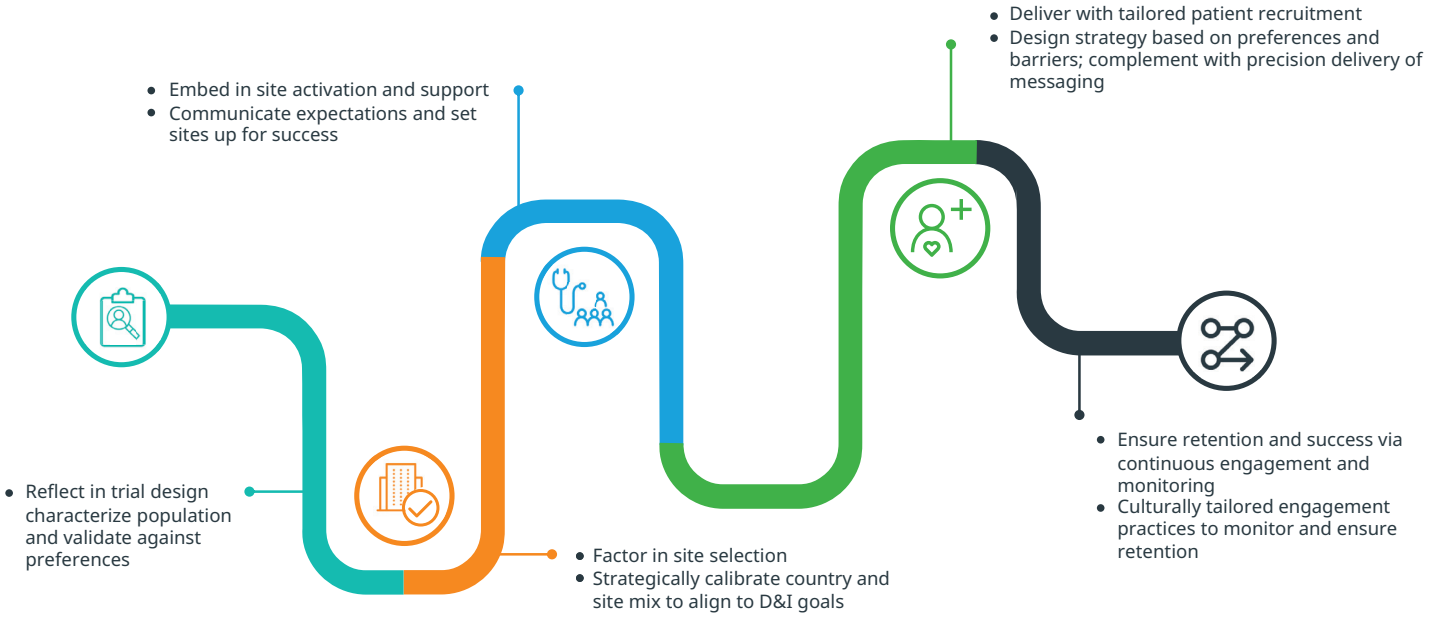

Figure 3. A lifecycle approach to achieving clinical trial diversity.

Conclusion

As oncology therapeutics development continues to be influenced by emerging biopharma and biotech companies, it's crucial to rethink oncology clinical trial strategy and find novel approaches compatible with the dynamic landscape.

Our teams understand the complexities present in the current environment. We ensure that these challenges are addressed with solutions integrated into the strategy and design of every trial we undertake with our customers. By doing so, we strive to deliver effective solutions that meet the demands of the ever-changing clinical trial landscape, ultimately progressing toward improved patient outcomes in oncology. We remain committed to advancing the field through thoughtful strategy, inclusive trial design, and cutting-edge technology.

About the authors

MURRAY AITKEN
Executive Director
IQVIA Institute for
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As head of the IQVIA Institute for Human Data Science, **Murray Aitken** provides policy setters and decision-makers in the global health sector with evidence, analysis, and insights that contribute to the advancement of Human Data Science to improve human health outcomes.

Murray is tasked with creating and managing a research agenda that leaders in global governments, payers, providers, academia, and the life sciences industry use to accelerate the understanding of global trends in disease patterns, data science, and technology. This research is used to foster innovation critical to evidence-based decision-making and the advancement of human health.

He holds an MBA, with distinction, from Harvard University and a Master of Commerce from the University of Auckland in New Zealand.

GERHARD DU TOIT
Global Oncology Head
IQVIA Biotech

As Global Head of Oncology, **Gerhard Du Toit** oversees all aspects of clinical project management to optimize strategic plans and enhance delivery for early and late phase oncology clinical trials. He is committed to delivering compliant, expeditious, ethical solutions that respect patient safety, meet GCP requirements, and add value to the needs of oncology customers. Working for several global clinical research organizations in his career, Gerhard is a seasoned healthcare executive with more than 25 years of experience in project, clinical and data management, business development and statistics.

ABOUT IQVIA BIOTECH

IQVIA Biotech delivers flexible clinical solutions designed to help biotech and emerging biopharma companies get treatments to patients. Our clinical development team brings expertise from two decades of planning and executing clinical trials exclusively for biotech companies. Drawing on IQVIA's unparalleled data and advanced analytics, IQVIA Biotech creates intelligent connections to deliver powerful insights to help customers accelerate clinical development of innovative medical treatments.

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