

ADVANCING EARLY-STAGE ONCOLOGY DRUGS: **PROGRESS, PRESSURE AND THE PATH TO BETTER TRIALS**

AT QPS WE BELIEVE IN DEVELOPING CLOSE AND LONG-LASTING RELATIONSHIPS WITH OUR CLIENTS ON THE BASIS OF TRUST AND MUTUAL RESPECT.

This mutual trust, combined with the agile approach we offer as a specialty CRO, helps improve the quality of your outsourced clinical work and reduces the degree of required oversight.



A RAPIDLY EVOLVING DEVELOPMENT ENVIRONMENT

Cancer remains one of the world's most urgent health challenges. Nearly 20 million new cancer cases and approximately 9.7 million deaths occurred worldwide in 2022. The annual number of new cases is projected to reach approximately 35 million by 2050, a 77% increase driven largely by population growth and aging.

At the same time, oncology research is producing an increasingly diverse pipeline of therapies. Advances in tumor biology, genomic profiling, immune regulation, drug delivery and biomarker technology have created treatment opportunities for patients whose cancers were previously difficult to treat. The challenge is translating this innovation into clinical benefit. Early-stage oncology studies must determine not only whether a therapy can be administered safely, but also whether it reaches its target, produces the intended biological effect, demonstrates early evidence of activity and can be developed at a dose patients can tolerate over time.

These questions are being asked within a difficult operating environment. Trials compete for small patient populations, protocols require specialized procedures, sites must coordinate complex testing and treatment schedules and sponsors must make major investment decisions using limited early data. This white paper will examine the scientific, operational and regulatory challenges shaping early-stage oncology development and the strategies sponsors can use to design more efficient, evidence-driven trials.

The Expanding Range of Oncology Therapies

Traditional cytotoxic agents remain important, but much of the current pipeline is focused on more selective or biologically directed approaches.

Targeted Small Molecules

Targeted therapies inhibit specific proteins or signaling pathways involved in tumor growth, survival or resistance. Current development increasingly focuses on uncommon genomic alterations, resistance mutations, synthetic-lethal targets and proteins once considered “undruggable.” These programs often require rapid molecular testing and a clear understanding of how target expression, resistance mechanisms and prior treatment influence response. Small biomarker-defined populations may create compelling opportunities, but they also make enrollment more difficult.

Antibodies and Antibody-Drug Conjugates

Monoclonal antibodies can inhibit tumor-driving pathways, activate immune mechanisms or deliver treatment selectively to cells expressing a particular antigen. Multispecific antibodies can engage more than one target or redirect immune cells toward malignant cells.



Antibody-drug conjugates combine a targeting antibody with a cytotoxic payload. Their development requires coordinated evaluation of antigen expression, linker stability, payload exposure, bystander effects, off-target toxicity and resistance. The antibody, linker and payload may each influence pharmacology and safety, making bioanalysis and exposure-response assessment particularly important.

Immunotherapies

Checkpoint inhibitors and other immune-modulating agents have transformed treatment across multiple cancers. New programs seek to improve response rates, overcome resistance and extend immunotherapy to tumor types that remain poorly responsive.

Early studies must account for immune-mediated toxicities, delayed responses, atypical imaging patterns and potentially prolonged biological effects. Combination strategies may improve activity but can make it difficult to determine which component is contributing to efficacy or toxicity.

Cell and Gene Therapies

CAR T-cell therapies have produced major advances in several hematologic malignancies, while tumor-infiltrating lymphocyte, T-cell receptor, natural killer cell and gene-edited therapies continue to advance. Research is increasingly directed toward improving durability, simplifying production, reducing toxicity and extending activity into solid tumors.

These trials require capabilities beyond conventional drug administration. Leukapheresis, cell processing, individualized manufacturing, product release, chain-of-identity controls, conditioning regimens and management of cytokine-release syndrome or neurologic toxicity must be closely coordinated.

Radiopharmaceuticals and Emerging Modalities

Therapeutic radiopharmaceuticals deliver radiation to tumor-associated targets and require expertise in patient selection, imaging, radiation safety, dosimetry and radioactive-product handling. The US Food and Drug Administration (FDA) has also issued modality-specific draft guidance addressing dosage optimization for oncology radiopharmaceuticals, reflecting the growing importance of this approach.

Other emerging approaches include cancer vaccines, oncolytic viruses, gene-editing products, RNA-based therapies and targeted protein degraders. Each modality presents distinct questions related to biodistribution, target engagement, manufacturing, immune response and long-term safety.

Dose Optimization Is Reshaping Early Development

Historically, many Phase I oncology trials were designed to escalate treatment until the maximum tolerated dose was identified. That approach was developed largely for cytotoxic chemotherapy, where greater exposure was frequently expected to produce greater antitumor activity.

For some modern targeted and immune therapies, doses below the maximum tolerated level may provide comparable activity with fewer adverse effects. The FDA's Project Optimus and its final August 2024 guidance emphasize selecting a dosage that balances efficacy, safety and tolerability rather than relying on maximum tolerated dose alone.

Sponsors may therefore need to evaluate more than one active dose and generate evidence from:

- ▶ Pharmacokinetic and pharmacodynamic analyses
- ▶ Exposure-response relationships
- ▶ Target-engagement and pathway biomarkers
- ▶ Comparative safety and tolerability
- ▶ Duration and intensity of dose interruptions or reductions
- ▶ Patient-reported symptoms and functional impact
- ▶ Cumulative or delayed toxicities
- ▶ Preliminary antitumor activity

Dose escalation and cohort expansion should form a connected evidence strategy. An expansion cohort is no longer simply an opportunity to treat more patients at the presumed recommended dose. It should help confirm whether the chosen dose is biologically active, clinically tolerable and suitable for longer treatment. This may require additional patients and more complex trial designs. Poor dose selection can create larger problems later, including avoidable toxicity, treatment discontinuation, protocol amendments, additional studies or regulatory delays.

Biomarker Precision Creates Recruitment Pressure

Biomarker-driven development can increase the probability of identifying patients likely to benefit. It can also divide common cancers into small molecular subgroups. Eligibility may depend on a rare mutation, an antigen-expression threshold, a genomic signature, a resistance mechanism, a previous treatment sequence or a combination of clinical and molecular characteristics. Patients may require archival tissue, a fresh biopsy, central confirmation or rapid genomic testing while their disease continues to progress.

Recruitment planning should begin before the protocol is finalized. Sponsors need realistic estimates of:

- ▶ Biomarker prevalence
- ▶ Availability and turnaround time of testing
- ▶ Expected screen-failure rates
- ▶ Competing studies recruiting the same population
- ▶ Geographic distribution of eligible patients
- ▶ Referral patterns and travel burden
- ▶ Site access to appropriate molecular diagnostics

Overly restrictive eligibility criteria can further limit enrollment and reduce the applicability of the findings. Criteria should be scientifically justified and aligned with the anticipated safety profile and mechanism of action, rather than automatically carried over from earlier studies.

Representative enrollment is also receiving greater regulatory attention. Recent FDA guidance encourages sponsors to consider eligibility criteria, enrollment practices and trial designs that support participation by populations more representative of the patients likely to use an approved therapy. The agency's June 2024 Diversity Action Plan guidance, which applies to specified clinical studies, remains in draft form.

Complex Protocols Require Stronger Execution

Many early-stage oncology protocols now include dose escalation, multiple tumor types, biomarker-selected expansions, alternative schedules, food-effect or drug-interaction assessments and combination arms. Safety decisions may depend on rapid integration of adverse events, laboratory results, imaging, pharmacokinetics, pharmacodynamics and biomarker findings. Delayed

or incomplete data can slow cohort review and create unnecessary risk.

Effective execution requires:

- ▶ Real-time participant and treatment-slot management
- ▶ Clear dose-limiting toxicity definitions and review processes
- ▶ Rapid reporting of serious adverse events
- ▶ Consistent imaging and response assessment
- ▶ Time-sensitive biospecimen collection and processing
- ▶ Coordination among sites and central or specialty laboratories
- ▶ Reliable data cleaning before safety-review meetings
- ▶ Documented decisions regarding escalation, de-escalation or expansion

Site selection must therefore consider more than historical enrollment. Sites need access to the correct patients, investigators familiar with the modality, appropriate treatment and laboratory infrastructure, trained staff and sufficient capacity to follow a demanding protocol.

Patient burden is equally important. Frequent visits, biopsies, imaging, blood collections, lengthy infusions and observation periods can discourage participation and increase withdrawals. Operational feasibility should be evaluated from the patient's and the sponsor's perspectives.

Translational Science and Bioanalysis Guide Decisions

Early clinical development increasingly depends on evidence that a therapy is behaving as intended. Sponsors may need to demonstrate that the drug reaches the tumor, engages its target, alters the expected biological pathway and elicits an immune or molecular response. This requires an integrated biomarker strategy that may draw on tumor tissue and circulating tumor DNA, as well as pharmacodynamic biomarkers, receptor occupancy assessments, cytokine measurements, immune cell profiling, immunogenicity testing and advanced imaging.

Assays should be developed early enough to influence dose and cohort decisions. Sample-collection timing, processing requirements, stability, shipping and analytical sensitivity should be established before enrollment begins. A scientifically valuable biomarker can become operationally useless if samples are collected inconsistently or results are returned after the relevant decision has been made.



Accelerated Development Requires Early Evidence Planning

The FDA's Accelerated Approval Program permits earlier approval of therapies for serious conditions based on a surrogate endpoint or intermediate clinical endpoint reasonably likely to predict clinical benefit. Confirmatory studies are required to verify the anticipated benefit. The agency may require a confirmatory study to be underway before granting accelerated approval, and its January 2025 draft guidance describes the factors it intends to consider in determining whether a trial is underway.

A successful expedited strategy therefore requires more than a promising response rate. Sponsors need a credible plan for dose selection, patient population, endpoint justification, manufacturing scale-up and confirmation of clinical benefit. Early regulatory engagement can clarify these expectations and identify gaps before they become expensive delays.

Advancing Better Oncology Programs

The most effective early-stage oncology programs integrate clinical development, biomarkers, bioanalysis, statistics, regulatory strategy, feasibility and operations from the beginning.

Across these challenges, early-stage oncology development should answer four core questions:

- ▶ Whether the therapy has sufficient evidence of biological and clinical activity
- ▶ Which patients are most likely to benefit
- ▶ Which dose and schedule offer the best benefit-risk balance
- ▶ What evidence is required for the next investment or regulatory decision

Scientific progress has created unprecedented opportunities in oncology. Turning those opportunities into therapies requires equally advanced planning and execution, grounded in the needs of patients whose time and treatment options may be limited.

QPS: A Partner for Oncology Drug Development

Oncology drug development requires more than identifying a promising target. Sponsors must show how a candidate works, how it behaves in the body, how it affects disease progression and how resistance may emerge.

QPS supports oncology sponsors across preclinical development, bioanalysis, translational research, clinical

pharmacology, regulatory strategy, clinical trial units and global clinical operations. By connecting these disciplines, sponsors can anticipate constraints, improve protocol feasibility, manage complex cohorts and produce decision-ready data.

QPS can help oncology drug developers with the following:

- ▶ **Nonclinical development support**
 - Generate data to characterize therapeutic activity, safety, exposure and development potential.
- ▶ **Bioanalytical method development and validation**
 - Develop reliable methods to measure drug candidates, metabolites, biomarkers and other critical analytes.
- ▶ **Pharmacokinetic and pharmacodynamic/ pharmacodynamic analyses**
 - Connect exposure to therapeutic activity, safety and dose selection.
- ▶ **Clinical development support**
 - Support studies across early- through later-stage clinical development.
- ▶ **Assay and biomarker strategy**
 - Align mechanisms of action with the right measurements for decision-making.
- ▶ **Regulatory-aware study execution**
 - Generate high-quality data packages that support development decisions and regulatory interactions.
- ▶ **Flexible CRO partnership**
 - Adapt to oncology programs across common cancers and rare diseases.

For sponsors navigating these scientific and operational demands, an integrated CRO partner can help connect biology, development strategy and trial execution. QPS brings scientific, operational and collaborative experience to help oncology drug developers move programs forward with confidence.

PARTNER WITH QPS TO OVERCOME EARLY-PHASE ONCOLOGY PROGRAM CHALLENGES

As outlined in this white paper, early-phase oncology studies face a variety of complex challenges. Navigating these obstacles requires a strategic approach, specialized expertise and robust infrastructure. QPS is well-positioned to assist sponsors in overcoming these challenges and advancing their early-phase oncology programs efficiently and effectively.

Extensive Experience with Early-Phase Oncology Studies

With a wealth of experience in conducting early-phase oncology trials, QPS has developed a deep understanding of the unique requirements and challenges associated with these studies.

Dedicated Early-Phase Research Facilities

Our global network of Phase I research facilities, comprising more than 500 beds, spans three continents. This extensive infrastructure allows QPS to conduct early-phase trials with a diverse and representative patient population, ensuring robust and generalizable results. The geographic diversity of our facilities also enhances patient recruitment and retention.

Skilled Team to Partner with Your Organization

Our team of skilled professionals, including clinical researchers, data scientists, and regulatory experts, collaborates closely with sponsors to understand their specific needs and goals. This partnership approach ensures that our strategies align with the sponsor's objectives, resulting in more effective and efficient trial execution.

Strategic Clinical Trial Planning

Strategic planning is at the core of our approach to early-phase oncology trials. We leverage our extensive experience and industry insights to design trials that are scientifically rigorous yet feasible. Our adaptive trial designs and innovative methodologies enable us to optimize study protocols, ensuring robust and reliable data while maintaining flexibility to respond to emerging findings.

Study Recruitment

Our comprehensive recruitment services, coupled with our global network of research sites, enable us to efficiently identify and enroll suitable participants. By ensuring that the right patients are included in the trials, we enhance the likelihood of successful outcomes.

Global Facilities and Staff

Our global presence, with facilities and staff across multiple continents, allows QPS to conduct multi-site, international trials seamlessly. This global reach not only enhances patient recruitment but also ensures that our trials adhere to diverse regulatory requirements and cultural considerations, making the findings more applicable and generalizable.

Regulatory Expertise

Our expert team has a deep understanding of the regulatory landscape across regions. We work closely with sponsors to prepare comprehensive submissions, conduct

regulatory gap analyses and engage with regulatory agencies, ensuring that all trials comply with the highest standards and proceed smoothly through the approval process.

CONTACT US TO LEARN MORE

Addressing the challenges and complexities of early-phase oncology trials requires thoughtful strategic planning and the implementation of quality systems and processes. By engaging with a partner with deep oncology expertise, sponsors can navigate these complexities, ensuring that their clinical trial journey is as efficient as possible.

Our proven success in the field has established our reputation as an innovative, results-driven partner. We encourage you to visit our website to learn more about our full range of support services for clinical trial sponsors.

Visit www.qps.com and discover how we can support your clinical trial. Contact us by email at infobd@qps.com or visit www.qps.com/contact.

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