

Insights Hub

# Key Approaches to Managing Protocol Complexity in Oncology Clinical Trials

Syneos® Health

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# Introduction

Early phase oncology has entered a new era. Scientific innovation is accelerating, but so is operational complexity. Sponsors are expected to optimize dose selection earlier, incorporate biomarker strategies, engage regulators sooner and generate stronger evidence while controlling timelines, costs and execution risk.

**Traditional development models were not designed for this level of scientific and operational complexity.**

Today, competitive advantage comes less from moving faster and more from making better development decisions earlier. This requires an operating model that connects scientific strategy, operational execution and real-time data from the beginning as a unified approach to development.

This playbook outlines four strategic levers that sponsors can use to modernize efficiency in early phase oncology clinical trials while maintaining scientific rigor and improving development execution.

## THE FOUR LEVERS OF MODERN EARLY PHASE DEVELOPMENT

### CLINICAL AND REGULATORY STRATEGY

Project Optimus, endpoint modernization, FDA engagement

### BIOMARKER-DRIVEN DESIGN

ctDNA[1]/MRD,[2] multi-omics, patient enrichment

### OPERATIONAL EXECUTION

Site strategy, patient identification, decentralization

### DATA + AI

Real-time data flow, AI decision support, workflow acceleration

1. ctDNA: circulating tumor DNA
2. MRD: minimal residual disease

Together, these four capabilities create a decision-making framework that helps sponsors reduce complexity, improve execution and generate stronger evidence throughout early phase development.

# Design Better Trials Before Complexity Takes Hold

## SPONSOR CHALLENGE

Early phase oncology has entered a new era. Regulatory expectations now extend well beyond establishing the maximum tolerated dose, requiring sponsors to generate stronger evidence sooner while balancing speed, scientific rigor and operational feasibility.

As protocols become more complex, clinical and regulatory strategies can no longer evolve independently. Decisions about dose optimization, endpoint selection and regulatory engagement must be integrated from the outset to reduce downstream risk, minimize costly protocol changes and support more confident development decisions.

## EXPERT PERSPECTIVE

**"Project Optimus has fundamentally changed how sponsors should think about early phase development. Success is no longer defined by identifying the highest tolerable dose; it's about selecting the optimal biologic dose that gives patients the greatest opportunity to benefit while generating the evidence needed for future development decisions."**

**Wael Harb, MD,** Head of R&D and Scientific Strategy, Early Phase Oncology at Syneos Health®.

## HOW LEADING SPONSORS ARE DESIGNING SMARTER STUDIES

Leading oncology sponsors are bringing regulatory strategy into study design much earlier than in the past. Initiatives such as the FDA's Project Optimus have shifted the focus from identifying the maximum tolerated dose to defining the optimal biologic dose, increasing the need for more adaptive, evidence-driven trial designs that can answer multiple development questions simultaneously.

Early engagement with regulators has become equally important. Discussions with the FDA on dose optimization, endpoint strategy and chemistry, manufacturing and controls planning help sponsors align development decisions with regulatory expectations before operational challenges emerge, reducing downstream uncertainty.

Rather than treating clinical development and regulatory strategy as separate activities, leading organizations are integrating them into a unified development approach that improves decision-making, reduces downstream risk and creates a stronger foundation for successful execution.

## KEY TAKEAWAY

Earlier regulatory alignment helps sponsors design stronger trials and make more informed development decisions.



### FEATURED RESOURCE

**Redefining Early Phase Oncology:** What Project Optimus Means for You

Learn how Project Optimus is reshaping dose optimization, adaptive trial design and early FDA engagement in this webinar.

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## FEATURED RESOURCE

**MRD as a Development Strategy:** The Paradigm Shift Reshaping Oncology Trial Design

Explore how MRD is evolving from prognostic marker to intervention trigger across oncology and what it means for trial design in this blog.



# Identify Appropriate Patient Populations Earlier to Support Trial Execution

## SPONSOR CHALLENGE

As early phase oncology protocols become more complex, identifying appropriate patient populations early is an important consideration in trial design and execution. Sponsors are under increasing pressure to identify responsive populations earlier, generate stronger evidence using fewer patients and make confident go/no-go decisions without extending development timelines.

Biomarker strategies have become essential to meeting those expectations, but only when they're designed to answer specific development questions rather than generate additional data.

## EXPERT PERSPECTIVE

**"The real power of biomarkers lies in turning biological insights into timely development decisions that move programs forward."**

**Jacquelyn Ritchie, MPH,** Therapeutic Area Head, Oncology/Hematology at Syneos Health.

## HOW LEADING SPONSORS ARE PUTTING BIOMARKERS TO WORK

Leading oncology sponsors are integrating biomarkers into trial design from the outset to improve patient selection, optimize dosing and evaluate treatment response earlier in development. Technologies such as circulating tumor DNA, minimal residual disease (MRD) and multi-omics are helping teams generate more precise evidence while reducing variability across study populations.

The most effective biomarker strategies are tied to specific development decisions, whether selecting patients, refining dose optimization or supporting response assessment. When aligned with these objectives, biomarker data becomes a decision-making tool rather than another endpoint to analyze.

Implementation, however, remains a challenge. As biomarker datasets grow more sophisticated, many organizations struggle to integrate complex biological insights into ongoing clinical decision-making. Success depends not only on scientific capability but also on operational processes that translate biomarker data into action.

## KEY TAKEAWAY

Biomarkers create value only when they drive decisions. The greatest advantage comes from integrating biomarker strategies into trial design early, ensuring that every data point contributes to better development decisions.

# Build Operational Strategy Into Trial Design From Day One

## SPONSOR CHALLENGE

Scientific innovation can only move as fast as operational execution allows. As early phase oncology trials become increasingly global, adaptive and biomarker driven, execution has become a strategic differentiator rather than simply a delivery function.

Yet, operational planning is often treated as something that begins after the protocol is finalized. When site strategy, patient identification and delivery models are considered too late, sponsors increase the risk of enrollment delays, protocol amendments and inconsistent trial execution.

## EXPERT PERSPECTIVE

**"The strongest oncology trials are designed for execution from the very beginning. Integrating site strategy, patient identification and delivery planning early creates more resilient, successful studies."**

**Pierre-Olivier Tremblay,** Global Lead, Clinical Pharmacology at Syneos Health.

## HOW LEADING SPONSORS ARE BUILDING FOR EXECUTION

Leading sponsors are designing operational strategy alongside clinical strategy, incorporating site selection, patient identification and decentralized capabilities before studies begin rather than layering them on later. This integrated approach helps reduce startup delays, improve enrollment and strengthen execution across increasingly complex global programs.

Patient identification represents an important opportunity to support trial efficiency. Sponsors are increasingly using electronic medical record (EMR) integration and hybrid or decentralized trial models to support earlier identification of potentially eligible patients, help reduce barriers to participation and support recruitment.

Operational innovation is also changing protocol design itself. Basket, umbrella and platform trials allow multiple research questions to be evaluated within a shared infrastructure, reducing duplication while generating evidence more efficiently. Together, these approaches help sponsors translate scientific innovation into successful trial execution.

## KEY TAKEAWAY

The strongest trials are designed for operational excellence from the very beginning.

## FEATURED RESOURCE

**Site Realities:** What It Takes To Deliver Clinical Trials Where It Matters Most

Explore how stronger site partnerships, operational planning and execution strategies help improve trial delivery and patient experience.



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# Turn Connected Data Into Better Development Decisions

## SPONSOR CHALLENGE

As early phase oncology becomes more data intensive, sponsors face a new challenge: making faster decisions without sacrificing scientific confidence. From patient selection and dose optimization to safety monitoring and operational execution, every critical decision depends on timely, reliable data.

Artificial intelligence can help accelerate development, but only when it is built on connected, trusted data and integrated into existing development workflows. Without that foundation, AI adds complexity instead of clarity.

## EXPERT PERSPECTIVE

**"AI isn't the strategy. Better development decisions are. The organizations that benefit most from AI will be the ones that first build the right scientific, operational and data foundations."**

**Wael Harb, MD,** Head of R&D and Scientific Strategy, Early Phase Oncology at Syneos Health.

## HOW LEADING SPONSORS ARE PUTTING CONNECTED DATA TO WORK

Leading sponsors are focusing on practical applications that improve development decisions, rather than adopting AI for its own sake. Connected data ecosystems that integrate EMRs, imaging, genomics and operational data allow teams to identify trends earlier, improve patient selection and support more informed dose optimization and go/no-go decisions.

AI is increasingly being used to streamline administrative activities such as protocol drafting, eligibility screening and regulatory documentation, allowing clinical teams to spend more time interpreting evidence and advancing development programs.

As adoption grows, strong governance remains essential. Trusted data, transparent models and clearly defined use cases will determine whether AI becomes a meaningful decision-support tool or simply another source of complexity.

## KEY TAKEAWAY

AI delivers the greatest value when it strengthens, not replaces, scientific judgment and clinical decision-making.



### FEATURED RESOURCE

**Early Signals at ASCO 2026 |** Can AI Finally Rebuild Clinical Research?

Understand why clinical research still relies on outdated workflows and how AI, electronic health records and real-time data are creating an opportunity to fundamentally redesign the clinical trial ecosystem in this podcast episode.

# Conclusion

**Modernizing Early Phase Oncology Starts With Better Decisions**

Leading sponsors are already moving toward a more integrated approach to development—one that brings together clinical and regulatory strategy, biomarker-driven trial design, operational planning and connected data from the outset.

Organizations that consistently outperform will integrate these capabilities from the beginning rather than treating them as separate functions. That means aligning clinical and regulatory strategy, using biomarkers to answer meaningful development questions, designing operational execution into the protocol and building connected data ecosystems that support timely, confident decision-making.

None of these capabilities creates value in isolation. Clinical strategy informs biomarker selection. Biomarker insights shape operational execution. Connected data transforms evidence into better decisions. Together, they create a more resilient operating model for modern early phase oncology.

As complexity continues to increase, competitive advantage will belong to sponsors that connect science, operations and data into a single decision-making framework—helping teams reduce uncertainty, improve execution and bring promising therapies to patients with greater confidence.

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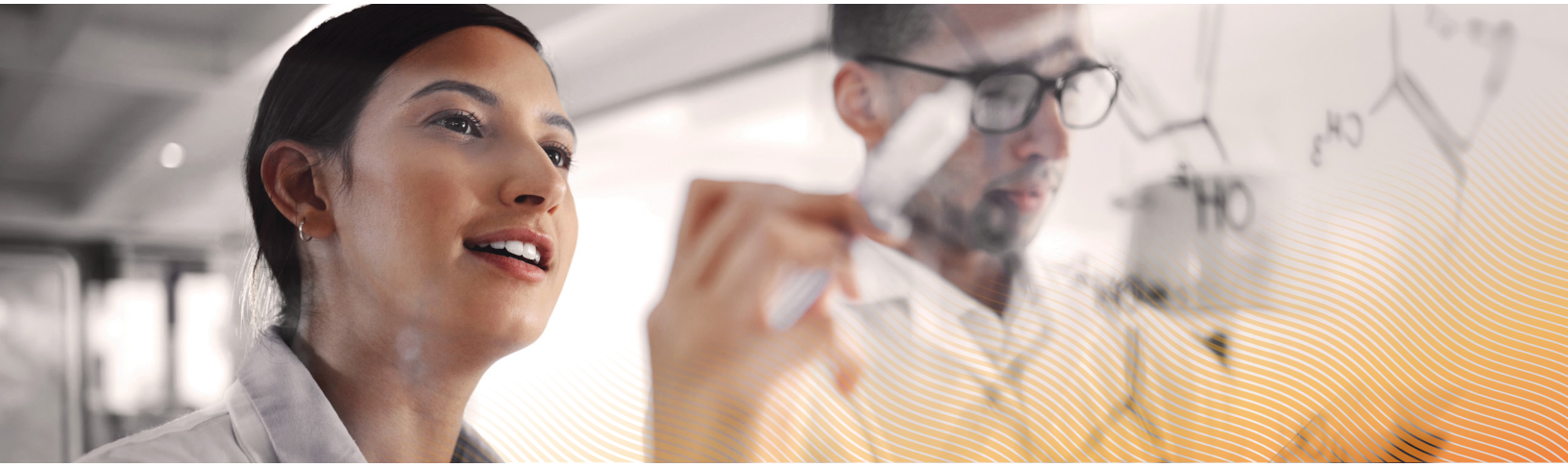
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## REFERENCES

1. DiMasi JA, Grabowski HG, Hansen RA. Innovation in the pharmaceutical industry: new estimates of R&D costs.*J Health Econ*.2016;47:20-33. doi:10.1016/j.jhealeco.2016.01.012.
2. Al-Madhagi HA. FDA-approved drugs in 2022: a brief outline. *Saudi Pharm J*. 2023;31(3):401-409. doi:10.1016/j.jsps.2023.01.007
3. Wong CH, Siah KW, Lo AW. Estimation of clinical trial success rates and related parameters.*Biostatistics*.2019;20(2):273-286. doi:10.1093/biostatistics/kxx069.
4. Wandile PM. Patient recruitment in clinical trials: areas of challenges and success, a practical aspect at the private research site. *J Biosci Med*. 2023;11(10):103-113. doi:10.4236/jbm.2023.1110010
5. Andrianov A. Two decades of rising protocol complexity: a longitudinal analysis of clinical trial design evolution, 2004-2025. *Appl Clin Trials*. Published June 23, 2026. Accessed July 2, 2026.
6. Syneos Health. *The Project Optimus Playbook: How to Build Smarter Early Phase Oncology Trials*. Published September 11, 2025. Accessed July 8, 2026. https://www.syneoshealth.com/insights-hub/project-optimus-playbook-how-build-smarter-early-phase-oncology-trials
7. Ritchie J, Harb W, Tremblay PO. *Rethinking Efficiency in Clinical Trials: Why Speed, Quality and Capital Don't Have to Compete*. Presented at FIERCE Biotech Week Lunch & Learn; May 12, 2026; Boston, MA.



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The Syneos Health Insights Hub generates future-focused, actionable insights to help biopharmaceutical companies better execute and succeed in a constantly evolving environment. Driven by dynamic research, our perspectives are focused on real answers to customer challenges to help guide decision-making and investment.

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