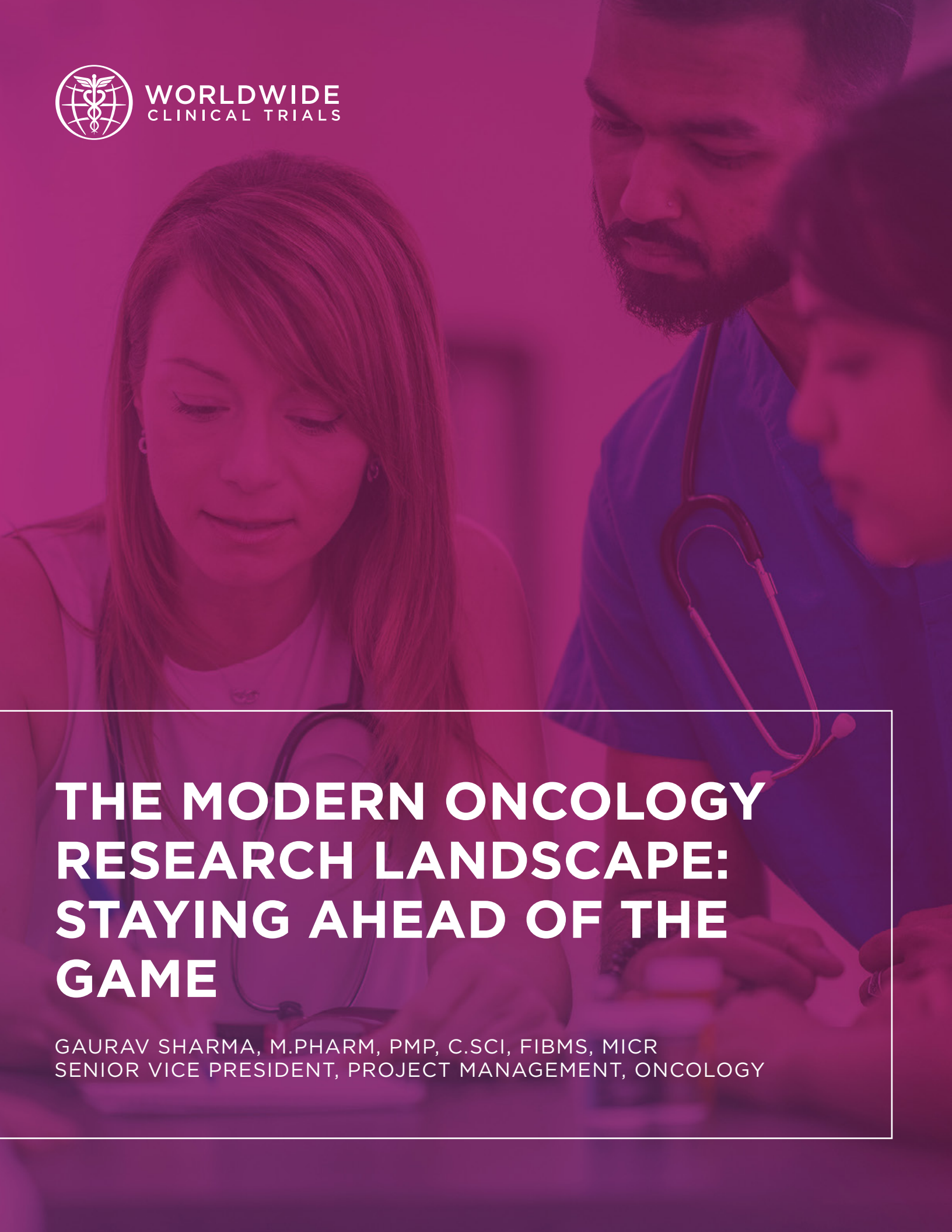


WORLDWIDE CLINICAL TRIALS

THE MODERN ONCOLOGY RESEARCH LANDSCAPE: STAYING AHEAD OF THE GAME

GAURAV SHARMA, M.PHARM, PMP, C.SCI, FIBMS, MICR
SENIOR VICE PRESIDENT, PROJECT MANAGEMENT, ONCOLOGY

THE "NEW" ONCOLOGY

Clinical development for oncology trials isn't what it used to be. Just between 2013 and 2018, the number of oncology drugs in late-stage development grew by 63%.[1] Newly launched drugs reached a record high in 2018, despite the overall success rate of fewer than 10% of all products entering development.

Although the landscape is competitive, companies that can position themselves strategically during preclinical explorations and throughout the development process can bolster their chances of achieving approval and market success. To do so, they must understand key elements of the "new" oncology research landscape:

- Diverse competition
- Increasingly complex trial design
- Targeted recruitment considerations
- Operational and regulatory requirements

CANCER THERAPY EVOLUTION

- Surgery
- Radiation
- Chemotherapies
- Stem cells

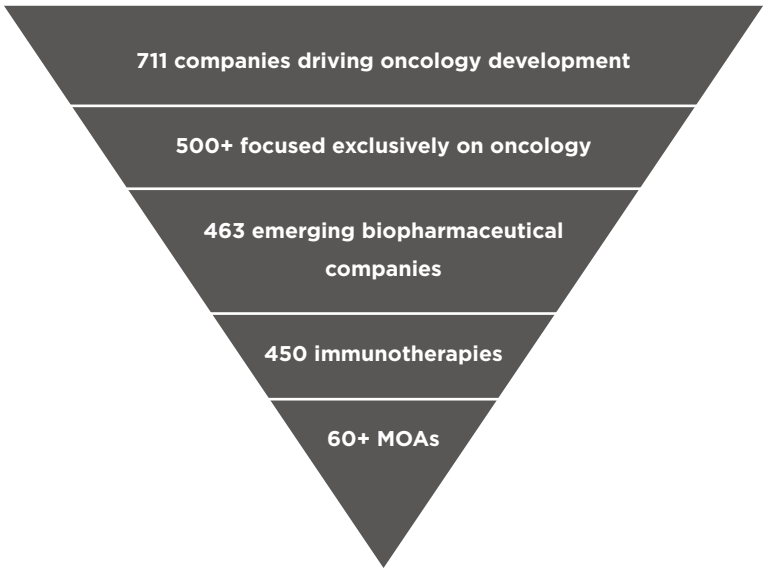
Immuno-oncology

- Immune checkpoint modulators
- Cell therapies * Oncolytic viruses
- Bispecific T-cell engagers * Peptide vaccines

DIVERSE DEVELOPMENT COMPETITION

The world of oncology development is no longer limited to the big players. Emerging biopharmaceutical companies make up a very large proportion of companies endeavoring to sell or launch the next big cancer drug. In addition to more than 60 mechanisms of action (MOAs) under investigation for about 450 immunotherapies, there are 98 "next-generation" biotherapeutics (cell, gene, and nucleotide therapies) under clinical investigation, with a further 18 MOAs being studied.

Strategic planning and early-stage concepting work is now increasingly important to companies hoping to reduce development risk and proceed through trials with few surprises and the best chance at commercializing their drug.



[1] All report data come from Global Oncology Trends 2019: Therapeutics, Clinical Development and Health System Implications. IQVIA Institute for Human Data Science. May 2019. Analysis and commentary are original to Worldwide Clinical Trials.

INCREASING TRIAL COMPLEXITY

Clinical trial complexity is measured as a combination of end points; eligibility criteria; and number of subjects, trial sites, and countries. In the past five years, Phase I trials alone have increased in complexity by 20%. Some of this complexity is driven by trial programs designed to incorporate larger numbers of indications per molecule. This is especially apparent in Phase I studies, which average 2.8 indications per molecule in 2018, compared to 1.6 in 2010.

While large biopharmaceutical companies have the accumulated knowledge and resources to accommodate these shifts, many midsize, emerging, and smaller biopharma companies can struggle to successfully juggle the design, analysis, and regulatory requirements for such complicated undertakings.

RECONFIGURED RECRUITMENT NEEDS

With a shift in trial design and end point complexity—as well as the nature of molecules under development—recruitment needs have dramatically altered. Instead of recruiting all comers as a heterogenous sample of adults with a single cancer (e.g., lung cancer, breast cancer), many trials now testing targeted therapies require homogenous populations with specific genetic tumor types or biomarkers.

New first-in-human (FIH) trial designs can facilitate swifter progression through Phase I and into Phase II studies, but the greater degree of monitoring for PD effects also means that drugs with limited desired biological impacts in early studies result in earlier Go/No-Go decisions. Trials that are not designed to enable smart progression and clear decision-making at this stage run the risk of early failure without good reason.

PAST: The "Cytotoxic" Age	**PRESENT: The "Targeted/Molecular" Age**
Dose to toxicity (maximum tolerated dose)	Dose to pharmacodynamic parameters (e.g., biologically effective dose)
FIH "3+3" design	FIH accelerated titration
Enroll "all comers"	Enroll specific tumor types
(heterogeneous sample)	(homogenous sample)
Predictive biomarker analysis	Predictive biomarker selection
Go/No-Go in Phase II	Go/No-Go in Phase I

MATCHING OPERATIONAL AND REGULATORY CAPABILITIES TO STUDY COMPLEXITY

With increasing trial complexity, operations and logistics must evolve accordingly. Companies can now optimize their pathways based on their development goals, provided they comprehend operational details such as:

By planning development programs with a thorough knowledge of the oncology operational landscape, companies can expect fewer interruptions and hurdles on the way to commercialization or mergers and acquisitions.

STUDY DESIGN

- Optimal study design options vary by phase
    - Cohort-based studies, standard design, and adaptive designs have unique uses

TRIAL LOCATION AND RECRUITMENT

- Locating and screening subjects is paramount to meeting recruitment targets
    - Strategic selection of sites and countries can determine program viability and return on investment
    - Access to the right network at the right time is essential
    - Infrastructure requirement for advanced therapies such as CAR-T or gene therapies
- Most oncology studies are performed at academic sites
    - Start-up with academic sites may be slower; a balanced mix between academic and commercial sites should be considered

TEAM EXPERTISE AND TRAINING

- Oncology-specific needs impact multiple functional areas and team responsibilities for trial conduct
- Site and staff training may require molecule-specific protocols and individualized education on PD and adverse event monitoring (e.g., American Society for Transplantation and Cellular Therapy Grading of cytokine-release syndrome and immune effector cell-associated neurotoxicity syndrome)

MONITORING AND REPORTING

- Monitoring and reporting requirements shift frequently and can result in a heavy reporting burden (e.g., for radiology, pathology, and data management)
- Independent Data Monitoring Committees (IDMCs) and Safety Monitoring Committees or Data and Safety Monitoring Boards (DSMBs) offer an additional layer of oversight for trial conduct
    - These boards often carry their own reporting and protocol requirements

SECURING A FUTURE IN ONCOLOGY

The rate of approvals per drug entering development is consistently lower than in other areas of medicine, but enthusiasm in oncology is perhaps better justified than in many fields. With its wealth of new screening techniques, targeted molecules, therapeutic strategies, and trial designs, patients and investors are rightfully optimistic that the future will hold more personalized, less-toxic treatments.

Companies that can seize the changing landscape and turn it into an advantage for their approach to drug development have the best chance at achieving their goals. Strategically align yourself with thoughtful, responsive research partners, such as the specialized oncology, end point, biomarker, adaptive design, and market access teams at Worldwide Clinical Trials.

Let Worldwide be your guide, from preclinical to post-market.

MEET THE AUTHOR

GAURAV SHARMA, M.PHARM, PMP, C.SCI, FIBMS, MICR
Senior Vice President, Project Management, Oncology

Gaurav is a strategic and tactical operations leader, with a wealth of experience building and managing high-performing teams and developing innovative, creative, and quality-driven solutions for clients. He brings strong and varied therapeutic expertise and strategic leadership skills, developed across franchise areas within several CROs and now to Worldwide. Prior to joining Worldwide, Gaurav was a Senior Vice President and Head of Global Project Management with Premier Research. He has worked extensively in solid tumor and hematological malignancies. More recently, Gaurav was responsible for overall successful delivery of clinical programs involving immune checkpoint inhibitors for the treatment of solid tumors and hematological malignancies.

Gaurav has also worked extensively in acute myeloid leukemia, cutaneous T-cell lymphoma and prostate cancer. He was program director a large program with tyrosine kinase inhibitor (TKI) involving several studies, including pivotal study for patients with EGFR mutated NSCLC, leading to marketing authorization. Gaurav is a Project Management Institute (PMI) certified Project Management Professional, a Certified Director by the World Council for Corporate Governance, and a Chartered Scientist (C.Sci) by the Science Council in the United Kingdom, with a wealth of experience working with pharmaceutical companies.