Line of Treatment: A Strategic Lever in Oncology Drug Development

Success in oncology drug development often hinges on decisions that are made well before the first patient is enrolled — and one of the most consistently overlooked variables is line of treatment. Whether a therapy is positioned in first-line (1L), second-line (2L), or later-line (3L+) settings can shape trial design, enrollment speed, competitive dynamics, and ultimately, probability of approval.

Our team has benchmarked historical performance across more than 6,000 oncology programs. By analyzing transition and success rates across treatment lines, phases, and tumor types, we provide strategic clarity on how this one decision — when to enter the treatment journey — affects a program's path.

Why Line of Treatment Matters

Line of treatment affects **everything downstream**: trial endpoints, comparator selection, patient availability, regulatory expectations, and market potential.

- **Earlier lines often face stricter scrutiny**: First-line programs typically require overall survival (OS) or progression-free survival (PFS) endpoints and must outperform well-established standards of care. This increases trial duration and complexity.
- **Later-line programs move faster but risk irrelevance**: 2L+ studies often rely on ORR or surrogate endpoints and enroll more quickly due to fewer available options. But they risk being leapfrogged by new 1L entrants before launch or reimbursement.
- **Regulatory incentives differ**: Later-line programs may be eligible for accelerated approval mechanisms, while 1L programs often face full data requirements — though successful 1L positioning generally translates into stronger uptake and market longevity.

Understanding the historical performance and tradeoffs across treatment lines can enable teams to **optimize trial strategy, portfolio allocation, and commercial timing**.

What the Data Shows

Our benchmark dataset provides a unique view into historical performance across treatment lines:

Category	Phase 1 Historical Approval Rate	Phase 2 Historical Approval Rate	Phase 3 Historical Approval Rate	Overall Historical Approval Rate	Phase 1 Transition Rate	Phase 2 Transition Rate
Oncology First-line	11%	12%	**35%**	13%	54%	28%
Oncology Previously treated	5%	9%	**35%**	5%	33%	17%
Solid Cancer First-line	10%	10%	**32%**	12%	56%	26%
Solid Cancer Previously treated	4%	7%	**30%**	5%	33%	14%
Liquid Cancer First-line	14%	21%	**46%**	17%	48%	36%
Liquid Cancer Previously treated	6%	15%	**48%**	7%	29%	22%

Key Insights

- **First-line programs progress better early**: Across oncology, 1L programs consistently show higher early-phase transition rates—especially in **solid tumors** (Phase I: 56% vs. 33%) and **liquid tumors** (Phase II: 36% vs. 22%). This likely reflects larger eligible populations, higher commercial value, and earlier sponsor commitment.
- **But Phase 3 success is strikingly similar across lines**: Despite the early-phase advantage, Phase 3 approval rates for 1L and previously treated programs are nearly identical in **solid tumors (32% vs. 30%)**, and even slightly favor later lines in **liquid tumors (46% vs. 48%)**. This suggests that once in pivotal stage, success is more tied to trial execution and differentiation than treatment line.
- **Hematology is the exception—not the rule**: In liquid cancers, first-line programs show stronger early-phase transitions and still perform well in Phase 3, but 2L+ programs actually edge them out on late-stage success. This reflects **targeted therapies** and **biomarker-driven designs** often tested first in refractory settings.
- **Later-line programs remain strategic entry points**: While Phase I and II transition rates are lower, 2L+ programs often benefit from **faster recruitment**, **less demanding comparators**, and **regulatory flexibility**—especially in high-unmet-need tumors.
- **Indication-specific context matters**: In hard-to-treat solid tumors like **pancreatic or brain cancer**, high attrition rates persist regardless of line. In these areas, **biologic targeting** and **modality innovation** may carry more weight than line-of-treatment strategy alone.

How We Support Decision-Makers in an Evolving Landscape

We support portfolio, clinical, and BD decision-makers by bringing clarity to how trial structure, treatment line, and historical outcomes interact across indications.

- **For clinical development teams**, we provide program-level benchmarks that inform endpoint strategy, comparator selection, and trial design — calibrated to treatment line and tumor type.
- **For portfolio strategists**, we map historical risk across phases and treatment lines to help prioritize LoT strategies that align with the asset's expected profile and timing.
- **For BD leads**, we contextualize whether an in-licensing opportunity is positioned to succeed — or whether it faces structural disadvantages based on where it enters the treatment journey.

By anchoring clinical strategy in historical data and predictive modeling, we give biotech leaders the clarity and confidence to act decisively.

Because in oncology drug development, success isn't just about when you enter—it's about knowing exactly what lies ahead.