Modality Momentum in Oncology: High Risk, High Reward Beyond the Usual Suspects

In oncology drug development, monoclonal antibodies (mAbs) and small molecule inhibitors (SMIs) continue to dominate the landscape, with over 9,500 historical clinical programs (comprised of interventional, industry-led, FDA-track clinical trials) to date. Their prevalence reflects decades of established safety data, clear regulatory pathways and operational familiarity. Unsurprisingly, both show relatively high Phase 1-to-Phase 2 transition success rates (33% each), likely due to well-understood risk profiles.

However, when it comes to late-stage progression and approvals, **newer modalities are quietly outperforming.**

Modality	Phase 1 to Phase 2 Transition Success Rate	Phase 2 to Phase 3 Transition Success Rate	Phase 3 Historical Approval Rate
Monoclonal antibody	33%	14%	35%
Small molecule inhibitor	33%	17%	32%
Antibody-drug conjugate (ADC)	33%	18%	54%
Bispecific antibody	13%	20%	60%
Chimeric antigen receptor T-cell therapy (CAR-T)	15%	46%	72%

Transition success rates and historical approval rates for the most common and some select trending modalities, at the clinical program level.

- **ADCs** now account for over **50% of all programs** across our "trending" modality segment (~1,000 programs total, consisting of the historical entirety of ADCs, CAR-Ts and bispecific antibodies). **Their Phase 3 approval rate stands at 54%,** significantly higher than that of mAbs (35%) and small molecules (32%).

- **Bispecific antibodies**, though still limited in volume, face the **lowest Phase 1 success rate (13% Phase 1 success)** among all modalities—but once they reach Phase 3, they boast a **60% approval rate**, the second-highest in this analysis.

- **CAR-Ts** show a **steep early-stage attrition rate (15%).** Yet their **Phase 2 transition success rate jumps to 46%**, and their **approval rate in Phase 3 peaks at 72%**, the highest observed across these modalities.

These benchmarks reveal a clear pattern: **while emerging modalities are risk-heavy upfront, their late-stage performance suggests significant risk discharging.** But that hinges on overcoming early development barriers—typically linked to manufacturing complexity, toxicity management and patient selection challenges.

Implications for Strategic Portfolio Planning

The data suggests that sponsors should re-evaluate risk–reward assumptions around less common modalities. Targeted investment in early-phase support for bispecifics, ADCs, and CAR-Ts could unlock disproportionately high value downstream if progression through Phase 1 and 2 is de-risked through better trial design and patient targeting.

Intelligencia AI: How We Fit Into the Equation

Our platform enables portfolio teams to:

- Benchmark transition and success rates across modalities, indications and phases, helping teams prioritize assets and investments based on empirical probabilities

- Identify where emerging modalities are most likely to succeed based on historical patterns, allowing for more focused development strategies and smarter risk allocation

- Apply predictive analytics as a bespoke service to optimize trial design and de-risk early-stage development

For companies willing to invest early and strategically, these trending modalities offer an outsized return on clinical risk.