EARLY-PHASE ONCOLOGY • 2026 EDITION

The Phase I/II Readiness Checklist

A structured self-assessment for biomarker-driven oncology programs

59 questions across eight domains, designed to surface the gaps that most often delay early-phase oncology programs — before a regulatory milestone, a partnering conversation, or a financing round surfaces them for you.

CellGene Nexus

Faster Paths from Lab to Life

Clinical trial design • Biomarker strategy • Regulatory & scientific writing

How to use this checklist

Work through it with the people who actually own each area — clinical, translational, biometrics, and regulatory in the same room. The value is not in the score. It is in the disagreements that surface when three people who assumed they shared an answer discover they did not.

Tick an item only if you could produce the supporting document or dataset today. An item you believe is handled, but cannot evidence, counts as unchecked. That distinction is the entire point of the exercise: diligence teams and regulators assess what you can show, not what you know.

Then count the unchecked boxes and read the interpretation on the final page.

What this checklist covers

SCOPE NOTE

This checklist addresses clinical development readiness — trial design, biomarker strategy, dose optimization, and the documentation that supports them. It does not cover chemistry, manufacturing and controls (CMC), which requires separate specialist review.

01 Scientific Rationale & Target Validation

Before design questions matter, the biological case has to hold. These are the items that surface first in partnering diligence and in early FDA interactions.

- [ ] Target expression or dependency demonstrated in at least two independent model systems relevant to the intended indication.
- [ ] Mechanism of action supported by direct pharmacodynamic evidence, not inferred solely from phenotypic response.
- [ ] Anticipated resistance mechanisms characterized — on-target mutation, bypass signaling, lineage plasticity, or efflux.
- [ ] Preclinical efficacy demonstrated at exposures plausibly achievable in humans.
- [ ] Combination rationale, where applicable, supported by evidence of synergy or non-overlapping toxicity rather than convenience.
- [ ] Competitive landscape mapped across the same target class, including agents currently in Phase I–III.
- [ ] Differentiation from the nearest competitor stated in a single sentence a non-specialist can repeat.
- [ ] Lead indication justified by biology and unmet need, not by enrollment convenience alone.

MOST COMMON GAP

A compelling preclinical package with no articulated resistance hypothesis. Both regulators and investors ask what happens at progression, and the absence of an answer reads as an incomplete development plan rather than an open scientific question.

02 Biomarker Strategy & Assay Readiness

For biomarker-directed programs, the assay is not a supporting detail — it is part of the trial design, and it governs whether the trial can enroll at all.

- [ ] Predictive biomarker hypothesis defined prospectively and clearly distinguished from prognostic markers.
- [ ] Biomarker threshold or cutoff pre-specified, with the supporting dataset documented rather than selected post hoc.
- [ ] Assay platform identified (IHC, NGS, ctDNA, flow cytometry, multiplex IF) with current analytical validation status recorded.
- [ ] Testing performed in a CLIA-certified and CAP-accredited laboratory wherever results drive enrollment decisions.
- [ ] Companion diagnostic co-development pathway assessed, with timing aligned to the registrational plan.
- [ ] Tissue requirements confirmed feasible at target sites — archival versus fresh, block versus slides, minimum tumor content.
- [ ] Assay turnaround time verified as compatible with the screening window written into the protocol.
- [ ] Contingency defined for indeterminate, failed, or quantity-insufficient samples.

UNDERESTIMATED RISK

Assay turnaround is one of the most reliable enrollment killers in precision oncology. A 21-day screening window paired with a 17-day average turnaround leaves no margin for shipping delays, repeat testing, or quantity-insufficient specimens — and each failure costs a patient who was otherwise eligible.

03 Patient Population & Eligibility Design

Eligibility criteria are where an elegant scientific plan meets the actual clinic. Every additional criterion narrows an already narrow pool.

- [ ] Eligibility reviewed against real-world biomarker prevalence in the specific line of therapy targeted.
- [ ] Prior-therapy requirements checked against current standard of care, which may have shifted since the protocol was drafted.
- [ ] Organ function and performance status thresholds justified by mechanism rather than inherited from a template.
- [ ] Washout periods reviewed for feasibility in a rapidly progressing population.
- [ ] Screen-failure rate modeled explicitly and built into enrollment projections.
- [ ] Impact of brain metastasis, prior immunotherapy, and comorbidity exclusions on the addressable pool quantified.
- [ ] Diversity and representativeness of the enrolled population addressed in a documented plan.

DO THE ARITHMETIC EARLY

A biomarker present in roughly 4% of patients in third line means screening on the order of 25 patients for every one enrolled — before any other exclusion applies. Model this before committing to a timeline, not after the first enrollment review.

04 Dose Optimization & Project Optimus Alignment

FDA finalized its guidance on optimizing dosage for oncology drugs in August 2024. Programs designed before that date frequently carry legacy assumptions that will not survive an end-of-Phase-II discussion.

- [ ] Development plan aims at an optimal biological dose, not solely a maximum tolerated dose.
- [ ] At least two dose levels planned for comparative evaluation ahead of the registrational study.
- [ ] Randomized dose comparison considered; where not feasible, the rationale is documented in the protocol.
- [ ] PK/PD and exposure–response data scheduled to be available at the moment of dose selection.
- [ ] Low-grade, chronic, and symptomatic toxicities captured — not only events inside the DLT window.
- [ ] Patient-reported outcomes incorporated into the tolerability assessment.
- [ ] Backfill cohorts or an equivalent mechanism used to build evidence at sub-MTD dose levels.
- [ ] Dose optimization strategy raised with FDA at an early development meeting.

THE SINGLE MOST LIKELY FAILURE POINT

A dose carried forward on maximum tolerated dose alone is now the most common reason programs are asked to generate additional data before a registrational trial. Retrofitting dose optimization after Phase II is substantially more expensive than designing for it.

05 Endpoints & Statistical Design

Early-phase trials exist to produce decisions. If the design cannot produce a clear decision, it will produce an expensive ambiguity instead.

- [ ] Primary endpoint matched to the phase and to the specific decision the study must inform.
- [ ] Response criteria specified (RECIST 1.1, iRECIST, or disease-specific), with investigator versus central assessment defined.
- [ ] Expansion cohort sample sizes justified by the precision required, not by convention.
- [ ] Interim analyses and futility rules pre-specified, including stopping boundaries.
- [ ] Multiplicity addressed explicitly wherever multiple cohorts, doses, or endpoints are involved.
- [ ] Go / no-go criteria written down numerically and agreed by the team before first patient in.
- [ ] Statistical analysis plan drafted before database lock — ideally before first patient in.

A USEFUL TEST

Ask your team to state the numeric result that would stop the program. If the answer takes more than one sentence, or if two people give different answers, you do not yet have a decision framework — you have a data collection plan.

06 Site Selection & Enrollment Feasibility

Site selection in biomarker-driven oncology is a different exercise from general oncology. Reputation is a weak predictor; screening infrastructure is a strong one.

- [ ] Sites selected on documented performance in the specific biomarker population, not on general institutional reputation.
- [ ] Site-level access to the required assay confirmed, including who pays for testing.
- [ ] Molecular tumor board or precision-medicine screening program relationships identified at each site.
- [ ] Competing trials at each site assessed for overlap with the same patient population.
- [ ] Per-site accrual modeled from historical performance data, then discounted.
- [ ] Startup timelines including IRB review, contracting, and budget negotiation built into the enrollment plan.
- [ ] Contingency sites identified in advance, rather than activated after enrollment falls behind.

WHERE TIMELINES SLIP

Enrollment projections built on optimistic per-site accrual are the most frequent single cause of timeline slippage in early-phase oncology. Sites with an active molecular screening program routinely outperform larger sites without one.

07 Translational & Sample Management

Correlative science is where early-phase trials generate durable value — and where they most often impose burden that quietly suppresses accrual.

- [ ] Each correlative objective tied to a specific development decision rather than collected speculatively.
- [ ] Sample collection schedule feasible within routine clinical workflow at participating sites.
- [ ] Paired baseline and on-treatment biopsies justified against the accrual cost they impose.
- [ ] Sample handling, shipping, and storage procedures written and tested before first patient in.
- [ ] Central laboratory and biorepository agreements executed ahead of activation.
- [ ] Data linkage between clinical and translational datasets planned at the outset, not retrofitted.
- [ ] Informed consent language covers intended future use of samples and genomic data.

A QUESTION WORTH ASKING

Mandatory on-treatment biopsies measurably reduce accrual. For each one, ask whether the result would change a development decision. If it would not, make it optional and protect your enrollment.

08 Documentation & Diligence Readiness

In partnering, financing, and regulatory interactions, documentation quality is read as a proxy for execution quality. That inference is usually correct.

- [ ] Protocol, investigator brochure, and informed consent internally consistent on dose, population, and endpoints.
- [ ] Investigator brochure reflects the current safety database rather than the version from the last submission.
- [ ] Protocol amendments anticipated, with a defined change-control process.
- [ ] Data management plan, eCRF, and edit checks aligned to the endpoints actually being analyzed.
- [ ] Trial registration and results-disclosure obligations tracked against deadlines.
- [ ] Publication and congress strategy defined, including authorship and embargo timing.
- [ ] A diligence-ready program summary maintained that a new reviewer could absorb in thirty minutes.

WHY THIS SECTION MATTERS MORE THAN IT LOOKS

Inconsistencies between protocol, brochure, and consent are among the first things a diligence team finds — and they raise questions about everything else in the data room.

Reading your result

Count the unchecked boxes out of 59. These bands are diagnostic rather than scientific — their purpose is to tell you where to spend the next quarter.

0 – 6 unchecked	**Well positioned** Your program is documented to a standard that will hold up in diligence. Focus on keeping the evidence current as the protocol evolves.
7 – 15 unchecked	**Targeted gaps** Typical for a program approaching first-in-human. The gaps are addressable, but they cluster — identify which domain holds most of your unchecked items and start there.
16 – 28 unchecked	**Material risk** Enough is unresolved that timeline and budget projections are unlikely to hold. Address biomarker readiness and dose strategy before committing to enrollment milestones.
29 – 59 unchecked	**Restructure first** The program is not yet ready for the milestone it is being pointed toward. A focused development plan review will cost far less than an amendment cycle or a failed cohort.

About CellGene Nexus

CellGene Nexus is a Houston-based scientific and clinical development consultancy working with emerging oncology companies on the questions this checklist raises. We anchor in the Texas Medical Center ecosystem and work with sponsors nationally.

Where we work

Clinical trial design	Phase I/II protocol development, dose optimization strategy, expansion cohort design, and endpoint selection for biomarker-directed programs.
Biomarker & stratification strategy	Predictive biomarker selection, cutoff justification, assay and companion diagnostic planning, and translational study design.
Regulatory & scientific writing	Protocols, investigator brochures, clinical study reports, abstracts, posters, and peer-reviewed manuscripts.

NEXT STEP

If a domain above came back mostly unchecked, send a short description of your program stage and the milestone you are working toward to **info@cellgenenexus.com**. We will respond with a specific suggested next step — or tell you plainly that your gap sits outside what we do.

Disclaimer. This checklist is provided for general informational purposes and reflects the authors' interpretation of publicly available regulatory guidance and common practice in early-phase oncology development as of 2026. It is not regulatory, legal, medical, or investment advice, does not create a consulting relationship, and is not a substitute for direct engagement with FDA or with qualified regulatory counsel. References to FDA guidance are the authors' summary, not an official statement of agency policy; verify current guidance before relying on any item.

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