RESTRICTED ACCESS

CASE-04 · PHARMA & CLINICAL DEVELOPMENT

Taking the drug «BX-204» to Phase III: €180 million over three years

The Phase II trial gave a positive, statistically solid result. Inside the company there's a push to start Phase III before the competitor.

THE JUDGMENT
Phase III → adaptive

CALIBRATED CONFIDENCE
44%

SECTOR
Pharma

EXECUTIVE VERDICT

The result is a **statistical mirage** — and the benchmark is about to change.

THE CALL	CONFIDENCE	IN ONE LINE
Phase III → adaptive	**44%**	Avoided a **€180M** trial potentially aimed at the wrong target.

§ THE PROTAGONIST & THE CONTEXT

The Chief Medical Officer of clinical development, with a €180 million program already in start-up and an executive committee demanding to move before the competitor reaches the finish line.

A mid-sized pharmaceutical company with a single molecule in advanced development. BX-204 is a candidate for a niche oncology indication — few patients, high unmet need, high expected price. The Phase III budget is the company's largest bet in the past decade.

§ BACKGROUND

The Phase II signal arrived unevenly: two of the twelve enrolment centers contributed more than half of the total response, and the biomarker-positive subgroup showed an effect almost double that of the general population. In oncology literature, this pattern — response driven by a few expert centers or a narrow subgroup — recurs regularly in Phase III failures: the effect does not replicate across the more heterogeneous population of large trials. At the same time, the main competitor has released preliminary data on an agent with a different mechanism of action that could redefine the standard-of-care protocol within eighteen to twenty-four months. If the reference comparator changes, the current trial design loses regulatory validity.

§ COUNTER-INTUITIVE SCENARIO

The result could be a **statistical mirage**. Much of the signal comes from a single patient subgroup and from two centers especially good at enrolling: on the true average, the effect is modest. And meanwhile a competitor is about to **change the standard of care** — the yardstick. You risk a €180 million trial aimed at a target that will soon no longer exist.

IMPLICIT ASSUMPTIONS

- The effect seen in Phase II is real and will repeat at large scale.
- The indicator measured now truly predicts patient benefit.
- The reference drug we compare against will remain today's.

FALSIFICATION TESTS

- Removing the two best centers, does the effect remain?
- In independent studies, does that indicator really predict the clinical outcome?
- How likely is the standard of care to change within 24 months?

QUESTIONS THAT RAISE THE BAR

- What is the real effect, once center and subgroup distortions are removed?
- If the standard of care changes, does the trial hold or must it be redone?

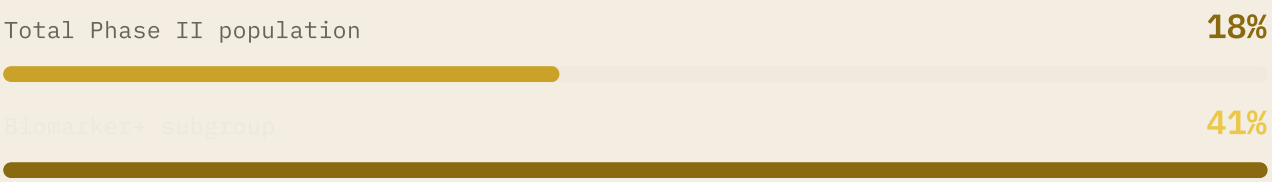
CALIBRATED CONFIDENCE & PROVENANCE

that the effect holds in Phase III as currently designed

Provenance: Phase II data (by center and subgroup) · literature on the indicator · competitor intelligence · red-team base.

BX-204 effect: all patients vs subgroup

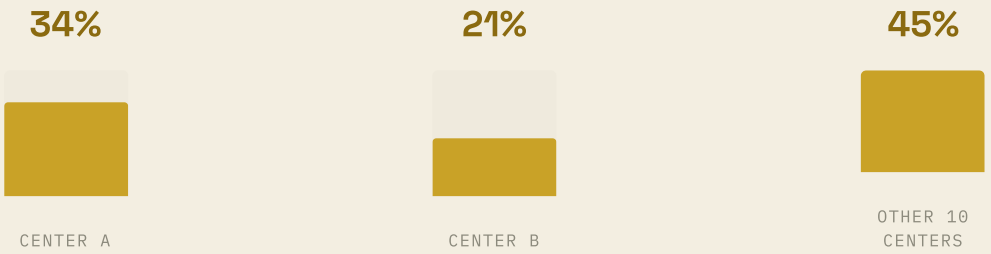
ILLUSTRATIVE DATA



Estimated relative response in the total Phase II population vs the biomarker-positive subgroup — the gap signals a non-replication risk (illustrative data).

Response contribution by center

ILLUSTRATIVE DATA



Share of total response attributable to each enrolment center — the two expert centers account for over half the overall signal (illustrative data).

OUTCOME

Adopted an **adaptive** design (one that adjusts on the fly) and updated the reference drug before full commitment.

VALUE

Avoided a **€180M** trial potentially aimed at the wrong target.

METHODOLOGICAL NOTE — READ FIRST

Composite cases, in the method of the Harvard Business Review: reconstructions based on real, recurring situations in each sector, merged and anonymized to protect confidentiality. The decision dynamics are authentic; names, figures and details are altered and not traceable to any single client or case. The «provenance» notes describe the type of evidence the engine cites with traceability in production. The Δ-CSI values illustrate the intensity of the pressure the contradiction put on the assumptions.