ARTICLE

Phase Ib studies. Speed vs. success: What should small biotechs weigh up before moving to patients?

A KEY QUESTION

Working with the right clinical development advisor/ally: How can small biotechs cut through early-phase complexity and decide whether a Phase Ib patient study will accelerate the right decisions?

KEYWORDS

Phase Ib Trials, Investor Pressure, Patient Recruitment, Healthy Participant Studies, Pharmacokinetics (PK), Pharmacodynamics (PD), Dose Selection, Biomarkers, Hybrid Phase Ia/Ib Design, Regulatory and Site Feasibility

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Smaller biotech companies often face intense pressure from investors to accelerate drug development by moving into patient studies as quickly as possible.[1] While Phase Ib studies in patients might appear to offer a tantalizing insight into potential signals of effectiveness, this approach can result in challenges, delays and additional costs, sometimes undermining the very speed investors demand.

This article explores the pros and cons of including patients early in clinical studies, highlights how different indications result in different strategies and offers practical guidance for biotechs to make informed decisions that balance speed, feasibility and long-term success.

De-risking Phase II or complicating Phase I?

Phase Ib trials sit between the traditional first-in-human ("Phase Ia") studies and the more expansive Phase II trials. Going beyond Phase Ia and its limited focus on safety and pharmacokinetics in healthy participants, Phase Ib introduces the investigational drug to patients with the target condition. The goal is to refine dosing, confirm safety in a real-world disease context and explore early signals of activity.

The growing interest in Phase Ib stems in large part from the pressure to accelerate development timelines and generate patient-relevant data earlier.[2] Sponsors and investors increasingly view these studies as a way to de-risk Phase II by validating assumptions sooner,[3] particularly for complex biologics or targeted therapies where healthy participant data may not translate well to patient populations. These studies also confirm the generation of data that can support an early sale or licensing of the product to other investors.

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The appeal of Phase Ib lies in its ability to provide actionable insights at a critical juncture. By enrolling patients (often following cohorts of healthy participants), these studies can uncover pharmacodynamic trends, biomarker responses and preliminary signals of activity that inform dose selection and trial design for later phases. They also enable early stratification of patient subgroups, which is particularly valuable in oncology and immunology, where heterogeneity can obscure outcomes.

For sponsors, Phase Ib appears to serve as a strategic shortcut—aiming to compress timelines by combining safety and exploratory activity assessments and sometimes paving the way for adaptive Phase Ib/II designs that regulators increasingly support.[4]

However, these studies are resource-intensive, requiring specialized sites, complex protocols and rigorous ethical oversight.

- **Recruitment can be challenging:** Patients can be reluctant to enroll in relatively short, and potentially sub-therapeutic dose level studies. Finding and enrolling patients can be time-consuming and expensive, especially when dealing with small, biomarker-defined cohorts[5]
- **Data validity should also be considered:** Data generated from limited sample sizes and sub-therapeutic doses may not provide the statistical power needed to guide pivotal decisions[6]
- **There is also a risk of introducing delays:** If Phase Ib becomes an additional step rather than a well-integrated part of the development plan

Sponsors must weigh the true value of the data against the cost and complexity, asking whether it adds meaningful insight beyond what a robust Phase II study could deliver.

The investor pressure: Speed at all costs? Speed at what cost?

For many biotech companies, the journey from discovery to clinical development is shaped not only by scientific ambition but also by the very real financial pressures that go with it.

Typically, progressing at this stage occurs through venture-backed funding. However, this can bring its own complications beyond the science—the need to show rapid returns and maintain confidence through demonstrating progress.

Safety, tolerability and PD are primary data, with market insights and therapeutic application combining to help build a comprehensive understanding of net present value.

However, this pressure to accelerate can obscure the practical realities of early-phase drug development. There can be an assumption that moving directly into patient cohorts will save time and impress stakeholders, however, this assumption is frequently misguided as acceleration is heavily dependent on the therapy area being targeted. Ultimately, it depends on the disease/condition as well as the landscape of existing available therapies. Phase Ib studies may be a great option in asthma but may be a poor choice in Alzheimer's or Muscular Dystrophy, for example.

In reality, the complexities of recruiting patients can introduce significant delays. Ethical considerations, logistical hurdles and the need for caretaker involvement can transform what appears to be a fast track into a protracted and costly process.

Moreover, the focus on speed can lead to strategic missteps, with companies risking incomplete or suboptimal data sets that may confound decision-making. The desire to satisfy investor demands must be balanced against the need for robust, actionable data and a feasible study design.

Ultimately, true progress is measured not by how quickly a company reaches its first patient, but by the quality and completeness of the data generated and the likelihood of successful advancement through subsequent phases. For biotechs, weighing investor pressure against scientific and operational realities is essential for long-term success.

Phase Ib: Not inherently synonymous with speed

Phase Ib studies in patients often sound like an attractive shortcut for biotechs under pressure to demonstrate clinical relevance. On paper, moving directly into patient cohorts seems to confirm faster insights and a compelling narrative for investors. In practice, however, the realities are far more complex—and may be counterproductive to the goal of speed.

Recruiting patients for early-phase trials is rarely straightforward. Consider Alzheimer's disease: finding suitable patient participants, securing caretaker consent and managing invasive procedures such as serial spinal taps can be daunting, especially when dose levels and study duration make it unlikely that the patient will experience significant or sustained clinical improvement.

Such logistical and ethical challenges can stretch timelines by months or even years—what appears to be a fast track instead risks becoming a bottleneck, possibly delaying critical data collection and increasing costs dramatically.

Enrolling patient cohorts is expensive; the cost of enrolling dozens of patients can far exceed that of healthy participant studies, potentially straining budgets and ultimately, investor confidence.

Certain situations (e.g., oncology trials with cytotoxic drugs) must be done in patients even at the first-in-human stage, as it would be unethical to expose healthy participants to such drugs. However, these situations are exceptions rather than the norm. For most therapeutic areas, starting with healthy participants offers a clearer, faster path to actionable data. Biotechs must recognize that Phase Ib in patients is not inherently synonymous with speed—it is a strategic decision that demands careful consideration of feasibility, cost and long-term impact.

A thought experiment on downstream decision making

One of the most clarifying questions that should be asked from a drug development perspective is whether or not the results from a small number of patient cohorts would change decision-making. Some possible scenarios are useful thought experiments:

- **Several cohorts of patients with idiopathic pulmonary fibrosis (IPF) follow on from multiple ascending dose cohorts of healthy participants for a promising experimental drug A that modulates fibrogenesis.**

  Scenario A: It is estimated that suppression of biomarker XYZ by >90% should result in a clinically meaningful result. In a cohort of 12 patients with IPF treated with the highest allowed dose level of drug A, levels of biomarker XYZ are suppressed by an average of 73%. Should the program be discontinued?

  Scenario B: In a cohort of 12 patients with IPF treated with the highest allowed dose level of drug A, levels of biomarker XYZ are suppressed by an average of 92%. Should an attempt be made to immediately sell or license the compound?

The case for traditional healthy participant studies

Delineating the PK properties of an experimental drug with a robust series of cohorts in healthy participants helps create a strong foundation for later phase trials. One of the most frequent errors in Phase II development is to insufficiently study the dose-effect relationship.[7] Anecdotally, it seems that there can be a tendency to more frequently fall into this trap when considerable time, effort and resources have been spent on a small number of patient cohorts in Phase Ib. While patient studies may seem like a direct route to clinically relevant data, healthy participant studies can provide a streamlined path to critical PK and safety insights, which form the foundation for intelligent dose selection and study design.

Healthy participants are easier to recruit, reducing timelines dramatically compared to patient cohorts. They also can eliminate many logistical and ethical hurdles, such as caretaker consent or invasive procedures that deter participation in patient populations. This simplicity can translate into faster enrollment, quicker data generation and lower costs—advantages that matter when resources are limited and investor expectations are high.

Healthy participant studies allow biotechs to lock down essential PK data before moving into patients, supporting more informed and efficient subsequent trials. Without this step, companies risk entering patient studies with incomplete knowledge, potentially leading to protocol amendments, wasted resources and potential regulatory setbacks.

Even in oncology—traditionally associated with patient-only early-phase trials—the trend is shifting. As newer, less cytotoxic therapies emerge, many sponsors may choose to begin in healthy participants to accelerate timelines and reduce costs. For most indications, this approach is not just pragmatic—it's strategic. By prioritizing healthy participant studies, biotechs can achieve true speed—the speed of successful, data-driven development rather than the illusion of progress.

Hybrid approaches: Balancing investor demands and scientific rigor

For biotechs caught between investor pressure and scientific best practice, hybrid study designs can offer a pragmatic solution. These approaches aim to blend the speed investors crave with the rigor required for meaningful data, helping to create a pathway that satisfies both strategic and operational needs.

A common hybrid model begins with a single ascending dose (SAD) and most multiple ascending dose (MAD) cohorts in healthy participants, where recruitment is faster and costs are lower. Once the foundational PK and safety data are secured, the study can incorporate a limited number of patient cohorts at higher doses. This design provides early patient exposure, addressing investor expectations while enabling future patient participation to be informed by robust preliminary data.

The benefits of hybrid designs extend beyond optics. By front-loading healthy participant data, sponsors can reduce the risk of protocol amendments and avoid wasting scarce patient resources on suboptimal dosing. At the same time, patient cohorts at the tail end of Phase I can deliver clinically relevant insights that can support investor narratives and regulatory engagement.

For smaller biotechs, hybrid designs represent a strategic compromise—not the fastest route on paper, but often the quickest path to actionable data and sustainable progress.

Regulatory and site considerations

Understanding the regulatory landscape is essential, particularly for smaller biotechs navigating complex global requirements.

In the UK, the Medicines and Healthcare products Regulatory Agency (MHRA) is widely regarded as consultative and pragmatic, offering sponsors a collaborative approach to early-phase trials. For biotechs seeking flexibility in study design, such as hybrid Phase Ia/Ib models, the UK can provide an accommodating environment, helping enable faster approvals and smoother execution.

Site capabilities are equally critical. In our experience, facilities with strong connectivity to academic centers, specialist investigators and patient referral networks can dramatically improve recruitment and operational efficiency.

Ultimately, regulatory and site considerations are not peripheral—they are strategic levers that influence timelines, cost and data quality. Choosing the right geography and collaborators can transform Phase Ib from a high-risk endeavour into a well-orchestrated step toward clinical success.

Success vs. speed: What really matters?

In early drug development, speed is often portrayed as the ultimate goal. For smaller biotechs under investor scrutiny, the pressure to demonstrate rapid progress can be overwhelming. Yet, the obsession with "first patient in" as a proxy for success is fundamentally flawed. True success is not about how quickly you start a patient study—it's about how efficiently you reach meaningful, actionable outcomes.

Rushing into Phase Ib without foundational data can create a cascade of problems—protocol amendments, recruitment delays and inconclusive results that stall development. What looks fast on paper can become years slower in reality. Conversely, a well-structured approach, beginning with healthy participant studies or hybrid designs, is much more likely to deliver the data needed to optimize dosing, satisfy regulators and maximize the value of every patient enrolled.[8]

Success should be measured by the speed of completing a study that informs the next step, not by the optics of early patient enrolment. This distinction is critical for biotechs navigating investor expectations. Educating stakeholders on the difference between perceived speed and actual progress can prevent costly missteps and preserve credibility.

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Ultimately, the question is not "How fast can we get into patients?" but "How fast can we generate the right data to move forward confidently?" For smaller biotechs, aligning strategy with this principle can be an effective way to balance urgency with sustainability—and to turn speed into success.

Conclusion

Phase Ib can be a powerful tool when deployed thoughtfully, but it demands clarity of purpose. The decision to run such a study should hinge on whether early patient data will materially influence development strategies, such as validating a mechanism of action, refining dosing or identifying responsive subgroups. Without that rationale, Phase Ib risks becoming an expensive detour rather than an accelerator.

In short, success depends on aligning scientific objectives with operational realities and engaging experienced collaborators who can navigate the regulatory, logistical and ethical complexities inherent in early patient trials.

A Practical Guide for Biotechs

For smaller biotechs, navigating the tension between investor expectations and scientific integrity requires a clear, actionable strategy. The first step is to acknowledge the pressure—investors often equate patient enrollment with progress, but this perception must be reframed. Educate stakeholders on the difference between perceived speed and actual development efficiency, using data and case studies to illustrate how rushing into patient studies can backfire.

Start by asking critical questions:

- Is early patient involvement truly feasible for your indication?
- Do you have the foundational PK and safety data needed to design an effective patient study?
- What are the regulatory and logistical implications of your chosen path?

If the answer to any of these is uncertain, healthy participant studies or hybrid designs that balance speed with rigor should be considered. These approaches satisfy investor demands for patient exposure while aiming to minimize risk and cost.

- Engage experienced collaborators early—CROs, regulatory consultants and clinical sites with proven connectivity to patient populations. Their knowledge can help you avoid pitfalls and identify opportunities for efficiency
- Leverage regulatory environments that favour consultative dialogue, such as the UK's MHRA, to help accelerate approvals without compromising compliance
- Finally, communicate proactively. Transparency with investors about timelines, risks and rationale can build trust and positions your company as disciplined and credible

In drug development, success is not about being first—it's about being right. By aligning strategy with this principle, biotechs can achieve speed that truly matters—the speed of sustainable progress.

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