HEALTH ADVANCES

Bioteching in action:

Five ways to attract early-stage investors

parexel® BIOTECH

“Investors told us they only fund a fraction of the start-ups that pitch to them: The most compelling ones can map a product’s or platform technology’s journey from basic science to commercialization.”

Biotech companies are a significant driver of innovation in drug development today, with a pipeline growing sharply in recent years. This growth provides hope for patients across many therapeutic indications. It also provides an avenue for future investment by financial institutions, industry partners, and investors.

For the last two years, the financial market has supported biotechs with record-shattering funding. While cash is key to short-term survival, drug development remains a long-term, complex endeavor. Companies with the discipline to interrogate their value story, analyze commercial opportunities from multiple angles, and leverage recent advances in clinical research will raise more money and increase their chances of delivering new treatments to patients who need them.

At Parexel Biotech, we help our clients every day by filling gaps in expertise, navigating global regulatory landscapes, and gathering diverse evidence sets using tools like decentralized trials and real world evidence. After conducting thousands of clinical trials, we know what it takes to reach the value inflection points that matter to investors. **We are bioteching with you.**

Our new survey of biopharma professionals who make investment decisions, reinforced by in-depth interviews with prominent investment firms, underscores how important it is for companies to tell a coherent, data-driven value story. We’ve identified five strategies to help them:

- Broaden your definition of unmet need
- De-risk your development plan
- Accelerate timelines with innovation
- Do your homework on potential investors
- Know your exit strategy and be flexible

We hope you find this new data helpful on your fundraising journey to help you **Never Stop Bioteching.**

Jim Anthony
Executive Vice President and Global Head
Parexel Biotech

Parexel Biotech research finds that biotech investors want a rigorous and multifaceted analysis of unmet needs, a realistic development plan, and a clear path to the next value inflection point

A hot market brings risks and opportunity

We are in a hot market for biotech, despite early signs that it may be beginning to cool down. The biopharmaceutical sector posted record financing, deal, and M&A numbers in 2020 and 2021, spurred in part by the swift and successful development of COVID-19 vaccines. Since the pandemic's beginning, average years of cash on hand for biotechs has risen from 2.1 to 2.7 years.[1]

An overheated market can increase risks for emerging companies. For instance, it may lessen the motivation to validate hypotheses fully or terminate mediocre projects. Likewise, investors and licensees may be less selective about funding and lower their due diligence standards.

Despite the risks, investor enthusiasm for biotech offers opportunities. Companies can raise more cash from capital markets and private placements, potentially sustaining years of development and shielding assets from a fickle marketplace. And they may have greater access to big pharma buyouts or partnerships. Companies can better seize these opportunities if they know what investors are looking for, especially in the early stages of development.

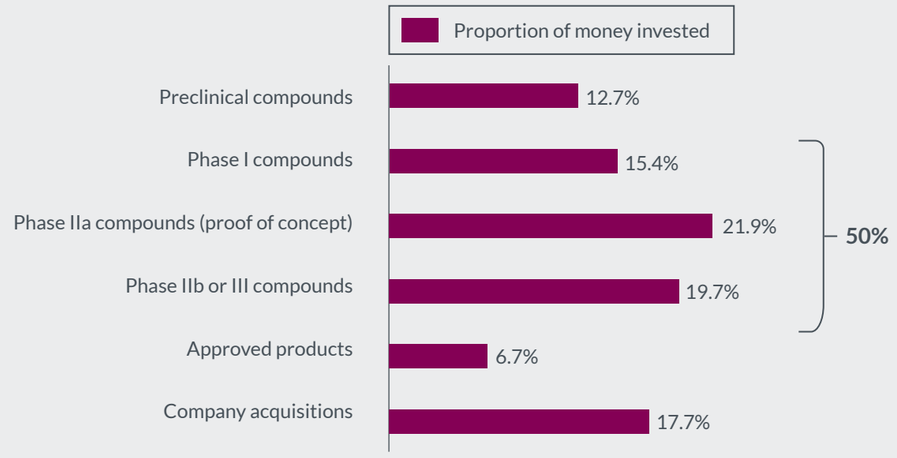
With this in mind, in November 2021, Parexel Biotech commissioned a survey of biopharma executives with decision-making responsibility for investments, acquisitions, and deals, supplemented by in-depth interviews with investment firms.[2] Our research shows that investors seek out early-stage compounds and prioritize those with reliable data that address a well-vetted unmet need. They told us they only fund a fraction of the companies that pitch to them: The most compelling ones can map a product's journey from basic science to commercialization.

[1] Jefferies Equity Research, Pharmaceutical Svcs., "August Biotech Funding: Eating into the Cushion," September 13, 2021.

[2] Survey of biopharma professionals from North America and Europe who evaluate internal and external compounds (and companies) for acquisition, in-licensing, or partnerships was conducted by Industry Standard Research (ISR), based in Raleigh, NC. ISR also conducted in-depth interviews with investment firms.

Investors prize early-stage assets with a data-driven value proposition

Exhibit 1. Half of the investment dollars go to preclinical and Phase IIa assets.



SOURCE: November 2021 investor survey conducted by ISR. Survey respondents were asked: "In dollar terms, what proportion of your biopharmaceutical investments are directed at individual compounds in preclinical or development stages, approved products, or at entire companies?". Amounts do not sum to 100% because some respondents gave incomplete responses.

The biopharma investors in our survey work for firms with annual R&D budgets over $500 million. They invest 70 percent of their biotech dollars in pre-commercial compounds, with half the funding going to those in preclinical, Phase I, or Phase IIa development (Exhibit 1).

On average, the biopharma survey respondents formally evaluate about 18 investment opportunities per year and invest in four of them (range: 0-20).

The investment firms that we interviewed said they increasingly focus on preclinical programs because of escalating competition among investors. "It's just gotten so much more competitive," one told us. "Before the last couple of years, our sweet spot was Phase I or II assets. Now it is preclinical, with about a year to the investigational new drug (IND) filing."

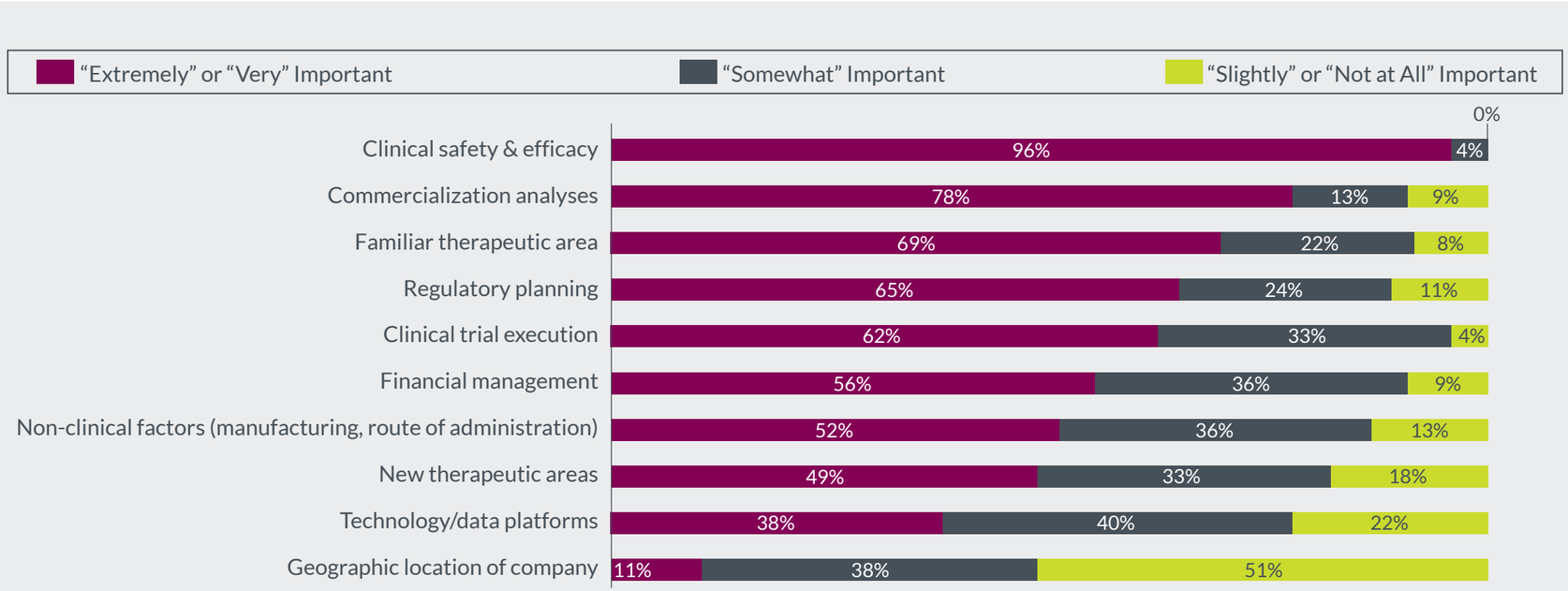
Investors said they funded just three to ten percent of projects they reviewed. "One hundred inbound pitches probably turn into ten that are decent," noted one. "After due diligence, we'll invest in maybe three of those." Another investor from a large firm confirmed that they rapidly narrow their focus: "We probably scan through 2,000 a year; last year, we made 15 new investments."

Biopharma investors ranked clinical safety and efficacy, commercialization potential, and a familiar therapeutic area (TA) as the top three attributes they look for in evaluating compounds for investment (Exhibit 2). Investment firms, who routinely evaluate compounds that have yet to enter the clinic, also say the target TA matters. "We like to operate in spaces where we have experience and prior success," said one respondent.

When asked to identify the single most important attribute, 58 percent of investors chose clinical safety and efficacy, 13 percent commercialization potential, and 4 percent clinical trial execution; familiar TA, financial management, and non-clinical factors were preferred by 2 percent of investors.[3] While 69 percent said it is extremely or very important that they have experience and expertise in the target TA, almost half place the same importance on expanding their portfolios to include a new TA.

When evaluating a company for acquisition, 64 percent of survey respondents say that one with a platform technology is more compelling than one with a single asset. The single most important criteria in evaluating companies for acquisition include clinical safety and efficacy data (51 percent), commercial strategy (18 percent), financial management and geographic location (4 percent each), and a new therapeutic area (2 percent). This suggests that many biopharma companies diversify their pipelines through acquisition.

Exhibit 2. Safety and efficacy, commercialization analyses, and therapeutic areas are critical attributes of candidate compounds.



SOURCE: November 2021 investor survey conducted by ISR. Survey respondents were asked: "When evaluating an investment in a particular compound, how important is each of the following categories?"

[3] ISR Biotech Investment Survey, November 2021.

5 strategies to attract early-stage investors and partners

To improve the long odds of bringing a new product to market, emerging companies must engage with multiple investors and partners from the earliest stages of development. We've identified five strategies to help emerging companies differentiate their value proposition to attract early-stage financing based on our online investor survey, insights from investor interviews, and our work with biotech clients.

1 Expand your definition of unmet need

Two primary reasons new products fail commercially are an incomplete understanding of the unmet medical need and lack of differentiation from existing treatments. Most companies know that new drugs and devices must fill an unmet patient need to achieve commercial success, but they may not consider the implication for funding. We found that the strength of the commercial strategy and analysis is a top consideration for investors (Exhibit 1).

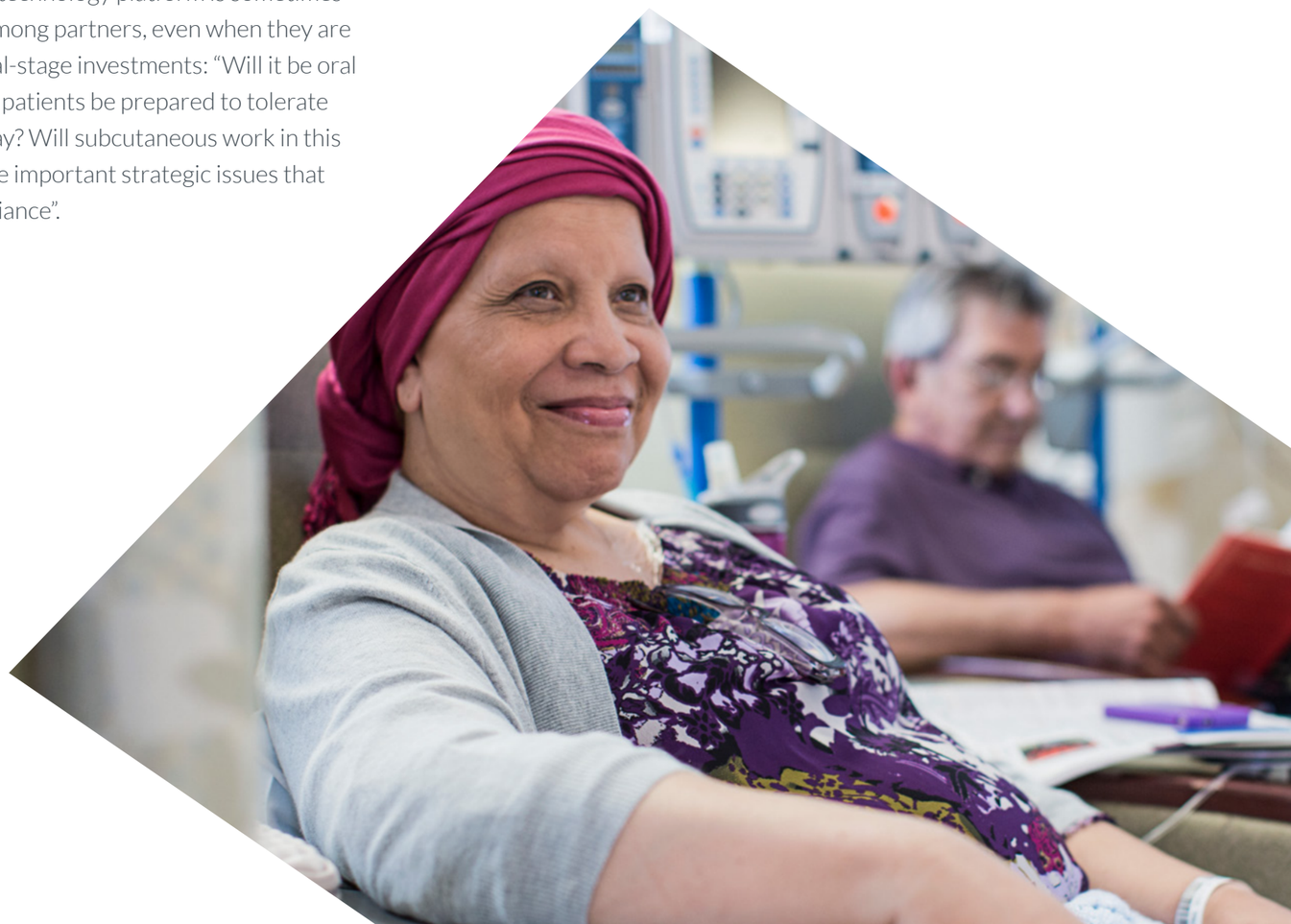
A significant unmet patient need is essential to establish a convincing commercial opportunity but is insufficient on its own. Companies must also consider:

- How differentiated is the product from current and future competitor treatments?
- What will drive physician uptake? Are the practice economics and logistics favorable?
- Are payers likely to provide favorable access to the product (e.g., low copays)?
- Will the cost of developing it permit a price point that aligns with the unmet need and is compelling relative to alternatives?
- Who are the most valuable target patients? What is the benefit-risk profile for various potential patient sub-segments?

Investors know that regulatory approval without reimbursement, swift or steady uptake, and sustained commercial viability won't deliver an attractive return on investment (ROI). Investors who plan to exit well before late-stage trials know a product's commercialization potential is key to attracting the next round of investors or a multinational partner, which is key to their ROI.

One investor told us that the route of administration of a new product or technology platform is sometimes an intense debate among partners, even when they are evaluating preclinical-stage investments: "Will it be oral or intravenous? Will patients be prepared to tolerate an injection every day? Will subcutaneous work in this indication? These are important strategic issues that affect patient compliance".

Even with diligent research, few early-stage companies can prepare certain answers to all the relevant questions about a commercial opportunity. But they can show they are aware of the complexities and multiple stakeholders involved. Answering as many questions as possible about how a product appeals to crucial stakeholders helps a company tell a compelling value story.



“Most companies know that new drugs and devices must fill an unmet patient need to achieve commercial success, but they may not consider the implications for funding.”

Commercial opportunity:

It’s not as simple as identifying an unmet need

There’s a clear unmet need in the United States for painkillers that are not addictive and have a better safety profile than commonly used opioids. However, even a product with a novel mechanism of action and an improved risk-benefit profile may not have a compelling value proposition in this clinical setting. Why?

- Opioids are potent and effective painkillers, so market entrants must also be potent.
- Traditional treatments such as high-dose acetaminophen, non-steroidal anti-inflammatory drugs (NSAIDs), physical therapy, acupuncture, and other approaches are effective for many patients.
- Pain treatments are typically orally administered, and patients may reject treatments they view as inconvenient, such as injectables.
- Most pain treatments are relatively cheap generics; thus, payers may apply significant scrutiny to novel high-cost treatments.

Failing to analyze an unmet need thoroughly could result in overblown estimates of market size and uptake trajectory. One investor interviewed said they specifically avoid companies that offer “hand waving” about the “total addressable market,” preferring a sophisticated presentation of the science and a detailed assessment of the potential patient population. Another respondent offered this advice: “You have to think about the patient first and why that patient now needs a new drug that will probably be more expensive than what’s out there. Of course, if there is nothing out there, then you have got a clear unmet need.”

2 Develop a strong plan, then de-risk it

Prospective investors and partners want to see a transparent, well-vetted data package and clinical development plan for your lead program. A poor or incomplete presentation can damage credibility, especially one that overestimates your probability of success. If, for example, you underestimate how much time and money it will take to get to the next value inflection, investors may wonder whether your clinical plan is flawed or if you have an accurate grasp of drug development in your target indication.

Even for very early-stage assets or platform technologies, your business plan should rely on sound science and data. Investors will likely find out during their due diligence if it doesn't. "We have PhDs on staff who kick the tires on the science and, once any investment gets to a certain point in due diligence, we hire outside experts to answer eight to ten key questions," explained one investor. "We call it 'peer review,' and we've walked away from deals based on those answers."

Early-stage companies that invest in comprehensive preclinical proof-of-concept (POC) work gain an advantage. Savvy investors and potential buyers look for pharmacological modeling and simulations of patient response as hallmarks of a high-quality, data-driven program.

Every investment firm we talked with said a top-notch Scientific Advisory Board (SAB) and collaborations with key opinion leaders (KOLs) provide external validation and de-risk investments. "If you have a Nobel laureate or Howard Hughes investigator on your [SAB], that matters to us," said one. "Those are surrogates for in-house talent." Investors say that licensing deals with major players are also valuable.

A development plan should include multiple milestones that will de-risk the asset. Although early-stage investors are accustomed to risk, they will parse it thoroughly before committing their money and time. For example, clinical POC data—potentially available at the end of Phase Ib/Phase IIa trials—is a major value inflection point because it reduces risk. Estimating the timing of that milestone requires deep expertise in clinical trial operations, expedited regulatory mechanisms, and the relevant therapeutic area. The timing for a first-in-class product with a novel mechanism of action will differ from that of a best-in-class product in a well-characterized disease.

Companies can also de-risk by offering a platform technology or diversifying their pipeline. Platform companies are desirable today, in part because they provide investors with multiple shots-on-goal. However, companies that assemble portfolios of attractive molecules based on their therapeutic area expertise have also been successful.

Understanding risks and planning for contingencies conveys competence: don't be afraid to discuss your backup plans if Plan A doesn't work out. Briefly, present well-considered Plan Bs, such as further testing the same drug in different diseases, to let investors know you are realistic and resilient.

3 Accelerate development with innovation

Recent advances in drug development tools and technologies can lower the risks and costs of bringing a new product to market—and investors know this. For example:

- The cost of DNA sequencing has plummeted in the last decade.
- Drugs developed using biomarkers are twice as likely to succeed as those that aren't.
- Machine learning, natural language processing, and artificial intelligence can accelerate medical literature reviews, optimize country and site selection for clinical trials, and speed enrollment by locating patients close to investigative sites.
- In silico modeling and contract research organizations (CROs) can help small companies complete initial trials without staffing up, while renting lab space and utilizing the cloud for processing and storing data can cut operating costs.
- Synthetic control arms (SCAs) can add power to early and small datasets and limit the number of patients who receive a placebo treatment.
- Surrogate and intermediate endpoints can shorten development timelines.
- Adaptive trials, basket trials, and decentralized clinical trials (DCTs) can streamline clinical research.

These powerful tools must be part of an integrated development plan. As one respondent explained, "We are asking, what can you prove in Phase Ib or IIa? If your strategy for a molecule requires a randomized controlled study and nobody will believe your data until then, it's going to be hard to make an efficient kill decision. There needs to be some basis for the target early, something you can see in a single-arm study."

Investors will reward companies that plan to go seamlessly from a Phase I dose-escalation study to a registrational trial because it shortens time to launch. But they must be confident a company can handle the complexities of shortened development, including manufacturing challenges and a leaner dataset for payers. A multi-year, high-quality natural history (NH) study may be the only way to establish a treatment standard for ultra-rare diseases. And a well-constructed SCA might eliminate the need for that NH study. However, if you plan to use an SCA, you'll need to ensure that data can be standardized and harmonized in your indication.

The COVID-19 pandemic showed that accelerated clinical development, remote trials, regulatory flexibility, and speedy agency reviews are possible. Investors are looking for companies that will utilize those tools.

4 Know your potential investors

> "Savvy investors and potential buyers look for pharmacological modeling and simulations of patient response as hallmarks of a high-quality, data-driven program."

Emerging companies that research their potential investors and partners can make more convincing arguments about why they are a good fit. Biotech investors and CEOs are a small community, so start-ups can ask around to gather intelligence about an investment firm's track record, portfolio companies, and investment philosophy.

That said, most companies will seize the opportunity to meet with an investor, even if they don't fit neatly into their investment strategy. A little research can go a long way in that scenario.

Most venture capitalists have a preferred investment round, such as Series A or B, or preferred initial investment size. A company with a preclinical asset seeking Series A financing won't get very far with an investment firm or corporate venture capital arm that places big bets on assets with clinical data in C and D rounds. Know who is in the room. Do they prefer details or generalities? Are they looking for an experienced management team? Do they invest in orphan drugs or platform technologies?

One investor told us that, for his firm, a platform technology company with a lead compound needs to demonstrate they can get to a clinical POC in three to five years for between $20 and $30 million. That's what's required to meet their ROI objectives.

Once a company has done the homework, it can tailor its presentation. For corporate venture capital funds, present a product development roadmap that fits the science of the drug and shows how your product fits into their portfolio. Know that investors don't like to think of themselves as simply a bank but rather as mentors and partners. Some investors can provide commercial strategic guidance and analytical support to refine a product's value proposition, identify attractive target patient populations, and evaluate the sales potential. They can pass on development experience from other start-ups in their portfolio to help interrogate the business plan. And they can connect young companies to networks of business, academic, or KOL clinicians with diverse TA and technical expertise.

The market is hot today, but it will cool down. As you assemble investors to fund your company through ups and downs, be thoughtful about who joins the team. As one respondent reflected, "In general, great teams are characterized by openness, transparency, positive energy, and high learning capabilities. As an investor, we know we will be working with the team for years and becoming almost family."

5 Reveal your exit strategy (but be flexible)

Investors want to understand your exit strategy, including the projected timing of significant value inflection points. A well-defined exit strategy will highlight your planning and preparedness for development and commercialization. Individual companies have different aspirations: some single asset companies look to be acquired before late-stage development, while some platform companies shoot for an IPO. Other companies want to be acquired before clinical testing begins so that the principals can move on to the next endeavor.

Make it easy for investors: Help them think through how much capital is needed and how long it will be committed to get to the next value inflection point. If you are doing a seed round or even Series A, you don't necessarily need to specify whether your ultimate aim is an IPO versus M&A. But in later funding rounds, you may have to discuss these plans. If you are upfront about your strategy, investors can determine whether they will be right for you. At the same time, be flexible about your exit thinking in investor meetings; present a plan and show you've thought about it while signaling a willingness to consider other options and adapt.

As one respondent told us: "To the best of your ability, display value inflection points like this; 'X millions of dollars will get us to this point, and this is the data that you'll see.' Nailing those down is extremely important."

"The market is hot today, but it will cool down. As you assemble investors to fund your company through ups and downs, be thoughtful about who joins the team."

Expertly

guiding early clinical strategies to place you on the path to success.

Advancing new and innovative science to address unmet needs often depends on securing early investments to drive the development of new treatments. Parexel Biotech and Health Advances can help you advance your strategy and development with consulting and clinical development services that are fully integrated and adaptable, giving you the right expertise and resources at the right time. We walk with you step-by-step through every decision, touchpoint, and milestone along your clinical development journey, so that together we can achieve your most important endpoint—bringing your innovation from the lab to the patients who need it most.
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Get the flexibility and adaptability it takes to never stop bioteching. ›

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About the Research

For this report, independent research firm Industry Standard Research surveyed >50 senior-level investment professionals representing fully integrated pharmaceutical companies and venture capital firms. The research included an online quantitative survey and qualitative interviews.