Health Advances

The Way Forward

Insights from the 2022 R&D Innovation Survey

parexel BIOTECH

QUO VADIS

Where are we going?
When will we get there?

Innovation is the lifeblood of the biotech industry. It has to be—new ideas and new ways of solving problems create pathways to conquering diseases. It is exciting, here at the start of 2023, to find our industry advancing a host of innovative therapies and applications that are transforming clinical development for the future benefit of patients worldwide.

And yet, the drug development environment is traditionally cautious with innovation. The adoption of new approaches can be a very long road. There is often a disconnect between the advancing therapies and the underlying technologies and processes that drive their advance.

The urgent needs posed by COVID-19 and the rising demand for new medicines have accelerated the use of three innovations that point to the future of clinical research: adaptive trial design, decentralized clinical trials (DCTs), and external control arms (ECAs). Due to advances in statistics, real-world data, artificial intelligence, and biosensors, these approaches have demonstrated their capabilities for high-speed, high-quality clinical evaluation in recent years. Social awareness of health disparities, regulatory imperatives and longstanding recruitment challenges are driving urgency for new methods to increase diversity in clinical trials.

So here in the post-pandemic landscape, we wanted to ask the question—where are we in terms of embracing these innovations? To what extent are biopharmas using adaptive designs, DCTs and ECAs? Are the new approaches being applied to the best effect with early planning? What benefits and barriers are researchers encountering in actual practice?

In this eBook, we share insights from 33 biopharma executives who reported their experience using these bellwether approaches for the *2022 R&D Innovation Survey* conducted by Health Advances and Parexel Biotech. This innovation snapshot shows biotechs adopting new approaches and encountering a variety of roadblocks, but pushing forward to expand their use and deliver faster, more efficient development.

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INSIGHTS

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Innovation Snapshot, 2023

Looking ahead, biopharma executives expect improved clinical development using novel trials designs, earlier integrated regulatory and commercial strategies, and greater diversity among research participants. Considered as a whole, findings from the December 2022 R&D Innovation Survey lead us to three top-line insights:

Regulatory and commercial strategies must be considered earlier.

- Clinical development often proceeds without sufficient consideration of regulatory and commercial strategy.
- Lack of early regulatory-commercial planning results in missed opportunities to reduce regulatory risks and optimize commercial success.

Adaptive designs, ECAs and DCTs are growing in importance.

- Despite their promise, applications are not always successful; biopharmas must thoroughly understand and plan early to use these approaches for optimal benefit.
- Biotech executives see increasing use of adaptive designs, ECAs and DCTs to accelerate timelines, reduce costs and mitigate risks.

Biopharma must pursue new ways to increase diversity in clinical trials.

- Established approaches to enhancing diversity (concierge services, community organization partnering) achieve only modest results.
- Long term, the clinical research community should begin developing research sites in wider locations that provide access to more diverse study populations.

BIOPHARMA IMPERATIVES:

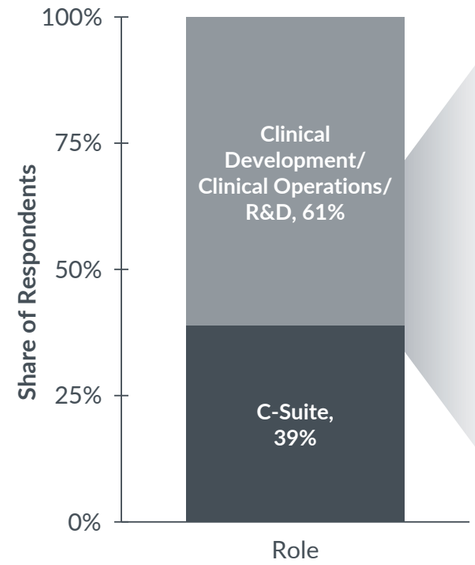
- Enhance market adoption
- Reduce risk of clinical and/or regulatory failure
- Speed new therapies to patients
- Reduce cost of development
- Increase diversity to deliver the most benefit for the most people

Respondent profile

In total, 33 biotech and pharma executives completed the survey, representing a mix of backgrounds and innovative trial design experience.

Respondent Titles

N=33, All Respondents

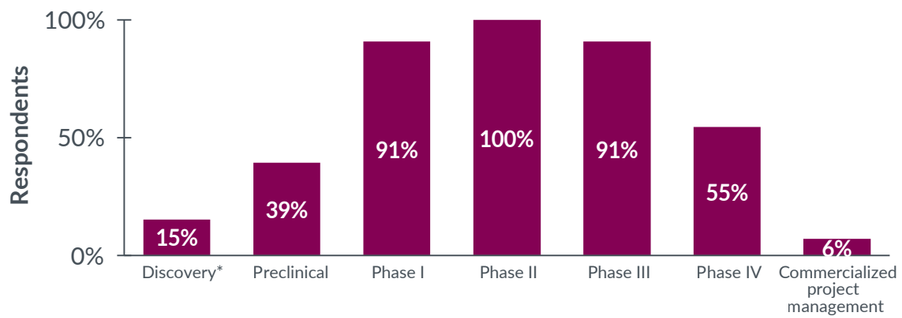


Broad Representation Across Phases of Development

Experienced with Innovative Designs and Approaches

Phases Under Purview

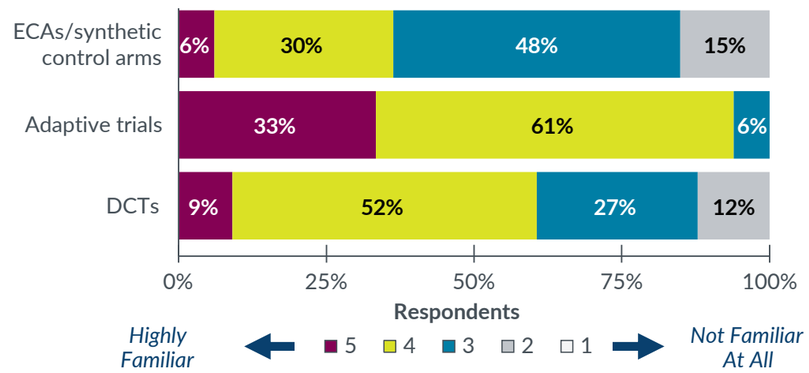
N=33, All Respondents



** Including target validation and lead compound identification/optimization.*

Familiarity with Innovative Designs

N=33, All Respondents



1 Biopharmas need earlier integration of commercial and regulatory strategies

When development proceeds without robust understanding of today's rapidly changing regulatory and commercial environments, we run the risk of developing a therapy that never reaches the patients it's intended to treat. We asked survey participants about the timing of their organizations' strategic planning and their satisfaction with current practices.

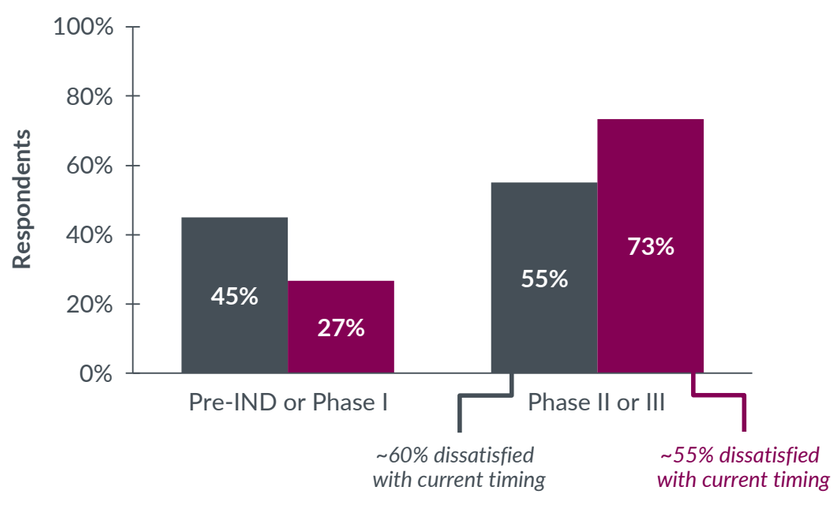
Early regulatory and commercial input positions products to address unmet medical needs, differentiate from competition, and collect evidence for rapid approval and market uptake.

What we learned:

- **Biopharmas typically consider commercial and regulatory strategy in late-stage development:**
  - **Commercial:** less than a third said commercial and market uptake planning were addressed in Pre-IND or Phase I.
  - **Regulatory strategy:** less than half said regulatory planning was considered in early stage development.
- **Most biopharmas who wait until late-stage development to engage with commercial and regulatory strategy are dissatisfied with that choice.**

Development Stage at Which Commercial and Regulatory Strategy is Considered

N=33, All Respondents



Source: R&D Innovation Survey, Health Advances survey and analysis

2 Overall satisfaction with innovative approaches is mixed

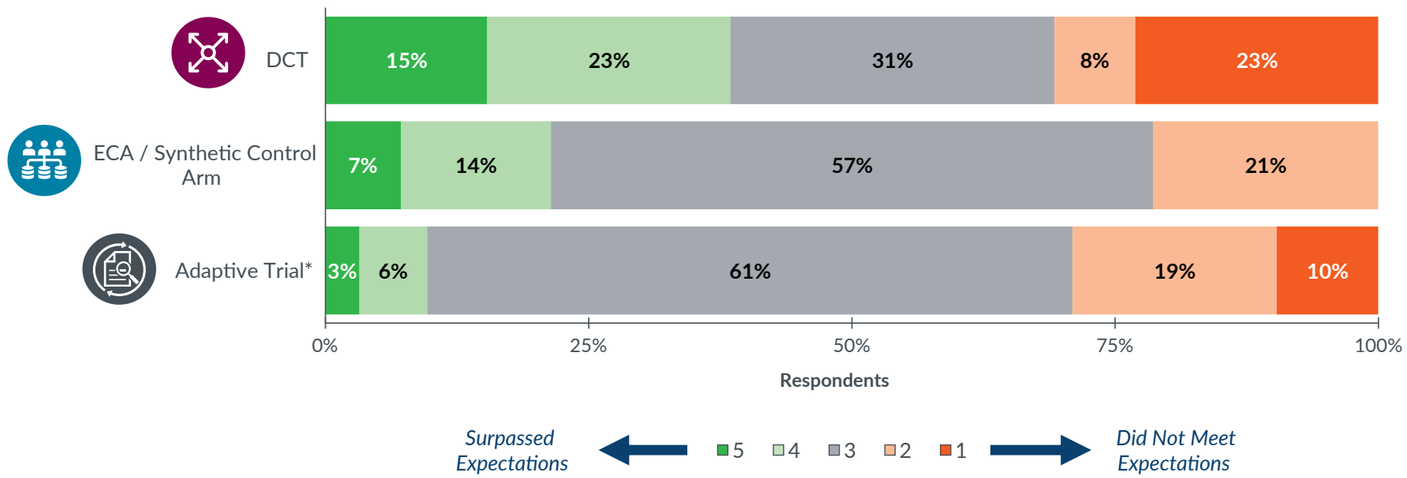
Respondent satisfaction with these innovative approaches was mixed. Nearly all of our 33 survey respondents had experience with adaptive designs (31). Fewer had used decentralized trials (22) and only 14 respondents reported experience with trials using external control arms.

What we learned:

- **DCTs** had the greatest disparity in satisfaction – notching the highest share of both satisfied (38%) and dissatisfied (31%) respondents.
- **ECAs** generally met expectations (57%): 21% were satisfied with their applications of external control arms, while 21% said ECAs did not perform as expectated.
- **Adaptive trials** generally met expectations (61%): 9% reported strong satisfaction, while 29% said adaptive trials failed to meet expectations.

Satisfaction with innovative clinical trial approaches is mixed

ECA / Synthetic Control Arm N=14
Adaptive Trial N=31
DCT N=22



**Including master protocol development, basket trials, umbrella trials, and platform trials.*

While many users of these approaches are satisfied, the application of these tools is not universally successful. **20% to 30% of biopharma executives noted poor experiences across trial designs and approaches.** Stakeholders need to thoroughly understand these approaches to take advantage of them and avoid pitfalls.

3 Common frustrations include patient retention/engagement and potential regulatory and commercial risk

Biopharma executives were highly positive regarding some benefits of the new approaches but also reported concerns and disappointments. Here's how they saw the advantages and barriers for DCTs, adaptive trials and ECAs.

What we learned:

DCTs

- On the plus side, data quality is better than respondents expected because DCTs can increase access to broader, more representative populations and outcome measures.
- But they tend to be disappointed by DCTs' ability to increase patient retention because the reduction of in-person visits can make it more challenging to identify and course-correct non-compliant patients.

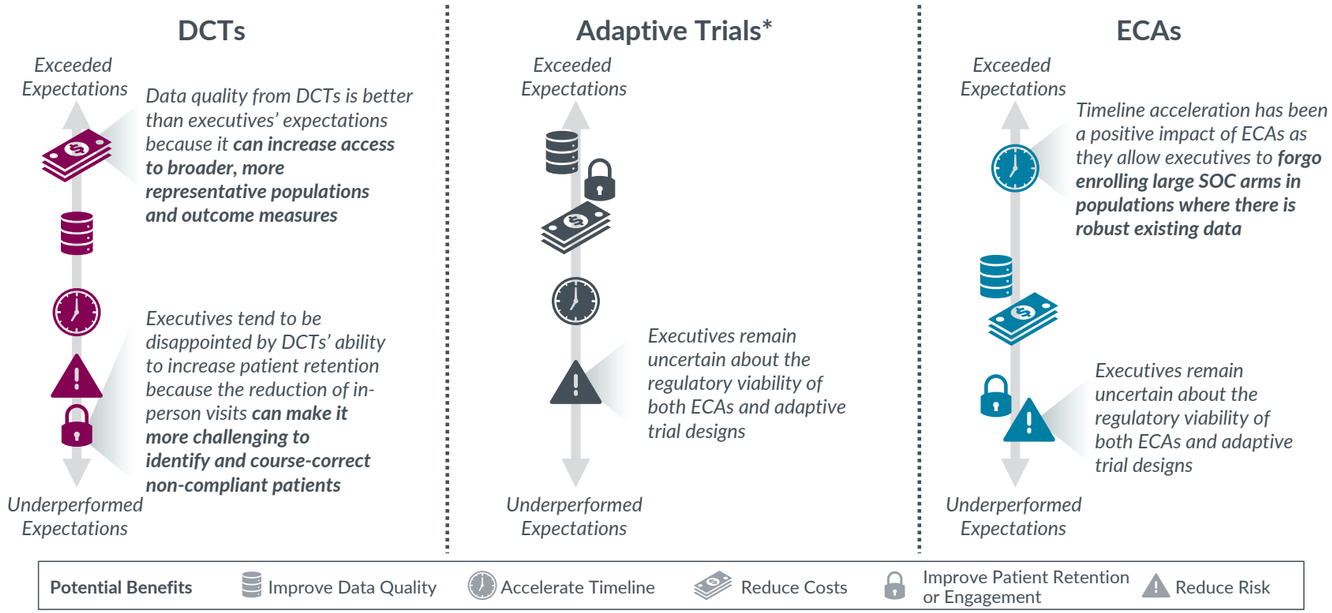
Adaptive Trials

- Executives are highly satisfied with quality of data from adaptive trials.
- However, they remain concerned about the regulatory viability of adaptive trial designs.

ECA

- ECAs have a positive impact on timeline acceleration since they allow executives to forgo enrollment for large standard-of-care arms in populations where there are robust existing data.
- Executives remain uncertain about the regulatory viability of ECAs.

Biopharma executives expressed frustrations with patient retention-compliance in DCTs; concerns with regulatory & commercial risks in adaptive trials and ECAs



4 Biopharma executives expect increasing use of adaptive designs, ECAs and DCTs

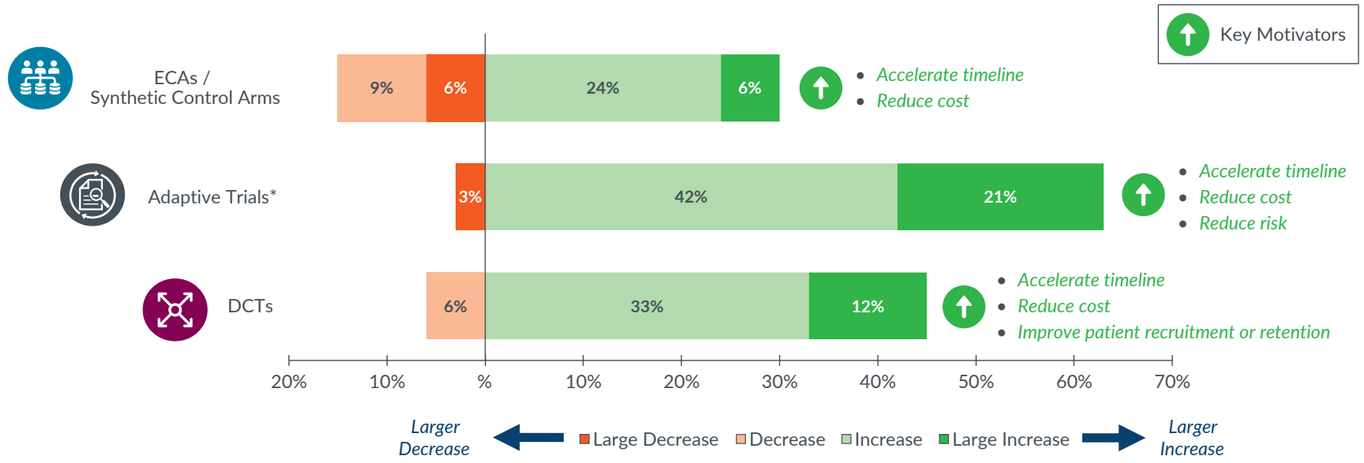
Biopharmas are highly motivated to use innovative clinical trial approaches to reduce cost and risk, and accelerate timelines. We asked them how they viewed the expansion of these approaches and what they saw as their chief benefits.

"Innovative trial design is an area of great interest to our company at the present time."

What we learned:

- **ECAs:** 30% of biotech executives expected increasing use of external and synthetic control arms because they expect this approach to accelerate timelines and reduce costs.
- **Adaptive trials:** 63% expected major increases in adaptive designs. They anticipate this approach will result in short timeline, reduced costs and risk.
- **DCTs:** 45% expected strong growth of decentralized trials. Together with reduced time and costs, they anticipate improved patient recruitment and retention from DCTs.

ECAs, adaptative trial designs and DCTs will become increasingly common
N=33, All Respondents



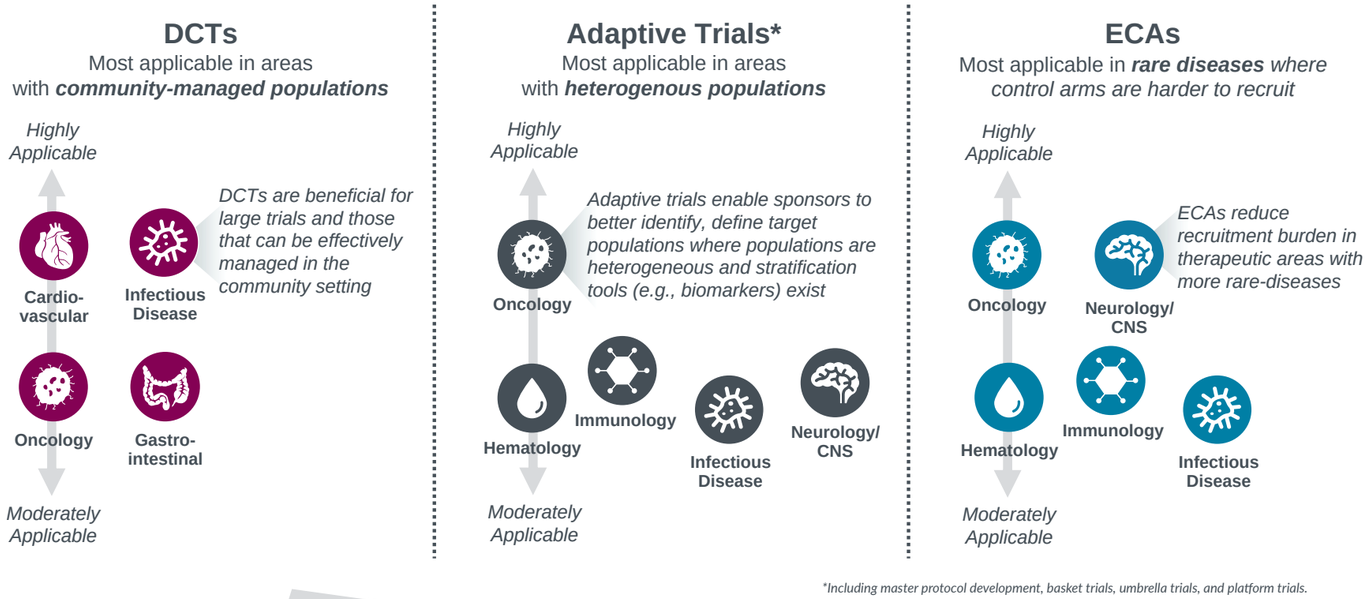
** Including master protocol development, basket trials, umbrella trials, and platform trials.*

5 Innovative approaches have most value in therapeutic areas with relevant characteristics

Our surveyed executives acknowledge that innovative approaches have broad applications. In current practice, though, they see the greatest value when an approach is thoughtfully applied to a trial based on the needs of the research setting and the population of interest.

What we learned:

- **DCTs** are beneficial for large trials and those that can be effectively managed in the community setting.
- **Adaptive trials** enable sponsors to better identify and define target populations where populations are heterogeneous and stratification tools like biomarkers exist.
- **ECAs** reduce recruitment burden in therapeutic areas with more rare diseases. Additionally, there is more acceptance among regulators for this approach in rare diseases due to the disease severity and challenges with recruitment.



*Including master protocol development, basket trials, umbrella trials, and platform trials.

Where are innovative approaches most useful?

DCTs are highly applicable in cardiovascular and infectious diseases and moderately applicable in oncology and gastrointestinal indications.

Adaptive trials are most applicable in therapeutic areas with heterogenous populations such as oncology, followed by hematology, immunology, infectious diseases and CNS indications.

ECAs: rare diseases

6 Establishing research sites in non-traditional locations is the best way to increase diversity long term

The survey asked biopharma executives to assess their experience using various approaches aimed at increasing diversity among clinical trial participants. Responses point to meaningful near-term solutions and the need for longer-term investment in research infrastructures to reliably reach underrepresented patient populations.

At least 30% of pharma and biotech companies see room for improvement in reaching underrepresented patient populations with evolving strategies for expanding clinical trial patient diversity.

What we learned:

Two commonly used approaches can increase diversity in the near term

- Patient concierge services were rated effective by 66%
- Partnering with community organizations was rated effective by 60%

Infrastructure investment will provide wider access in the long term

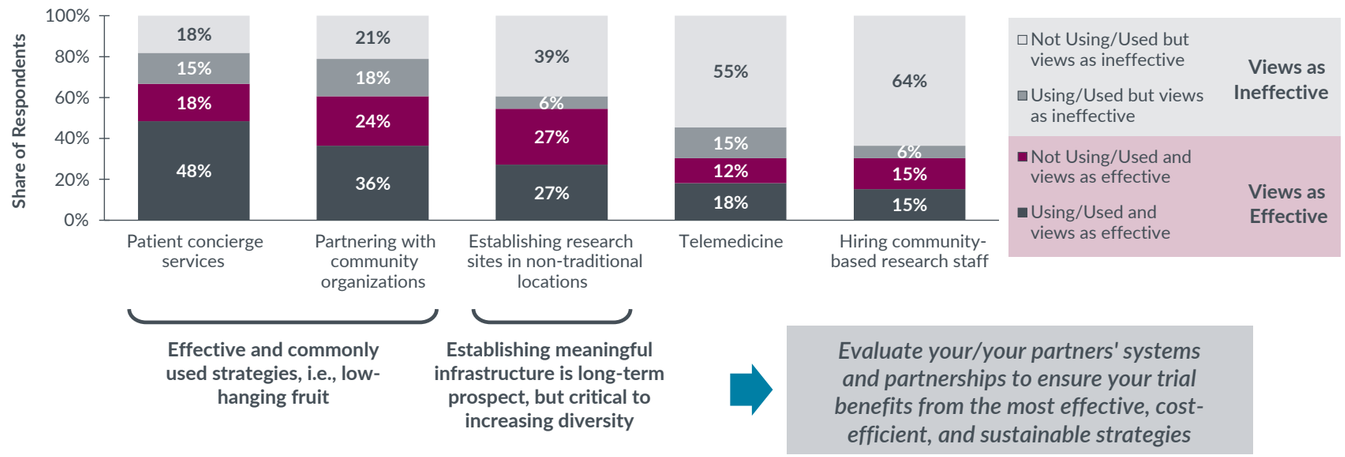
- Establishing research sites in non-traditional locations was an approach deemed effective by 54%

Two approaches were seen as ineffective

- Telemedicine was reported ineffective by 70%
- Hiring community-based research staff was reported ineffective by 70%

Biopharma executives identified several promising approaches to increasing diversity in clinical trials

N=33, All Respondents



From “what if” to “what’s next”

Innovation begins with a vision.

- What if we could simulate ‘virtual’ patients for drug evaluation?
- What if we could collect data while study participants go about their daily lives?
- What if we could use early findings to guide a study to a more robust, meaningful conclusion?
- What if the people participating in trials accurately represented the diversity of patients who have the potential to benefit from these new therapies?

Adaptive designs, decentralized trials and external control arms—novel approaches sparked by these imaginings—are now being deployed by biopharma researchers dedicated to making them work in actual practice. Results of the 2022 R&D Innovation Survey tell us how well they are working and where they yield the greatest benefits.

What’s next? Responses from biopharma executives also tell us what’s needed to harness the new approaches for more efficient, more patient-focused development. Biopharma will be learning how to identify the best approaches for a given study; how to better engage with study participants to ensure compliance with remote data-collection protocols; how to understand and mitigate regulatory risk and optimize commercial opportunities; and how to reach underrepresented patient populations. All of which will require earlier integration of commercial and regulatory planning.

For additional insight and discussion, join Parexel Biotech and Health Advances’ companion webinar series. Our experts provide a mix of strategic guidance and practical how-to advice on design and appropriate use of adaptive designs, DCTs, ECAs and approaches for expanding clinical trial diversity.

Evaluate your/your partners’ systems and partnerships to ensure your trial benefits from the most effective, cost-efficient, and sustainable strategies

With Heart™

Jim Anthony

Executive Vice President, Global Head Parexel Biotech

Jim has over 25 years of pharmaceutical industry experience, and 22 years of CRO Experience. Since 2019, Jim has applied a key tenant of his leadership style, “go the extra mile”, to lead the Parexel Biotech division. Known as a change agent who keeps the patient at the heart of everything he does, Jim has defined what excellence in leadership looks like and driven the success of this fully dedicated and cross-departmental division.

In 2022, PharmaVoice recognized Jim as a member of their “PharmaVoice 100,” a distinguished group of honorees who are pushing the industry forward.

As Global Head of the Biotech division, Jim works closely with executive leadership teams in small, emerging, and mid-sized customers, providing guidance to help them stay at the forefront of industry trends in clinical development so their work makes a deep and lasting impact.

Mike Davitian

Vice President, Health Advances

A leader in Health Advances’ Biopharma and CNS Practices, Mike has broad therapeutic area expertise and over 10 years’ experience in growth strategy, business development (including partnering, licensing and M&A strategy), commercial due diligence, digital solutions, and product and portfolio optimization. Before joining Health Advances, he has experience in Healthcare Investment Banking at Inverness Advisors, LLC, Stanford Financial Group, and Thomas Weisel Partners.