ROUNDTABLE SUMMARY

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Pharma Ignite | SCRIP CITELINE COMMERCIAL

Overcoming Obstacles & Seizing Opportunities in Early Phase Biotech Research

Colin Orford, Senior Vice President Drug Development Services, ICON Biotech
Juliane Bernholz, CEO, AM-Pharma
Andrea Chicca, CEO and co-founder, Synendos Therapeutics
Peter Lichtlen, Chief Medical Officer and Co-founder, Numab Therapeutics
Lars Nieba, CEO, Engimmune Therapeutics
Gerd Arold, Senior Director Scientific Affairs, Clinical Pharmacology, ICON Biotech

Moderator: Daniel Chancellor, VP of Thought Leadership, Norstella

KEY TAKEAWAYS

- Survey participants highlighted different challenges at different stages of development.
- In navigating these challenges, biotechs often prefer to retain core scientific capabilities internally, but perceive great value in forming external relationships for activities they can't do on their own.
- When selecting a CRO, biotechs have several selection criteria, including medical expertise, transparency, global capability, flexibility, agility and speed.
- Biotech leaders see potential for CROs to provide value in ways that go beyond CROs' traditional value proposition.

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OVERVIEW

At every stage of development, biotechs see the need to retain certain critical scientific capabilities internally. However, biotechs also understand the need to outsource and partner for other activities, such as market research, commercial analysis, compliance and regulatory activities, and operational tasks, especially related to clinical trial recruitment and trial implementation.

In deciding which organizations—particularly contract research organizations (CROs)—to partner with, biotechs have developed a set of criteria that includes experience and expertise, global capabilities, governance, the expertise of team members, and more. In addition, some biotechs are looking for greater value from CROs that goes beyond their operational expertise and includes medical expertise and strategic input in areas such as clinical trial strategy, inclusion/exclusion criteria, and protocol development, especially in certain therapeutic areas. Demonstrating expertise in these areas will often influence the decision on CRO selection.

CONTEXT

In conjunction with a survey by Citeline and ICON of 149 representatives from biotech companies about the challenges they face—*Early Phase Development: Understanding Key Obstacles for Biotechs in 2024*—Citeline also convened a panel of biotech leaders in Basel, Switzerland. The panelists described challenges they are dealing with and shared their perspectives on when and why they work with external partners, such as CROs.

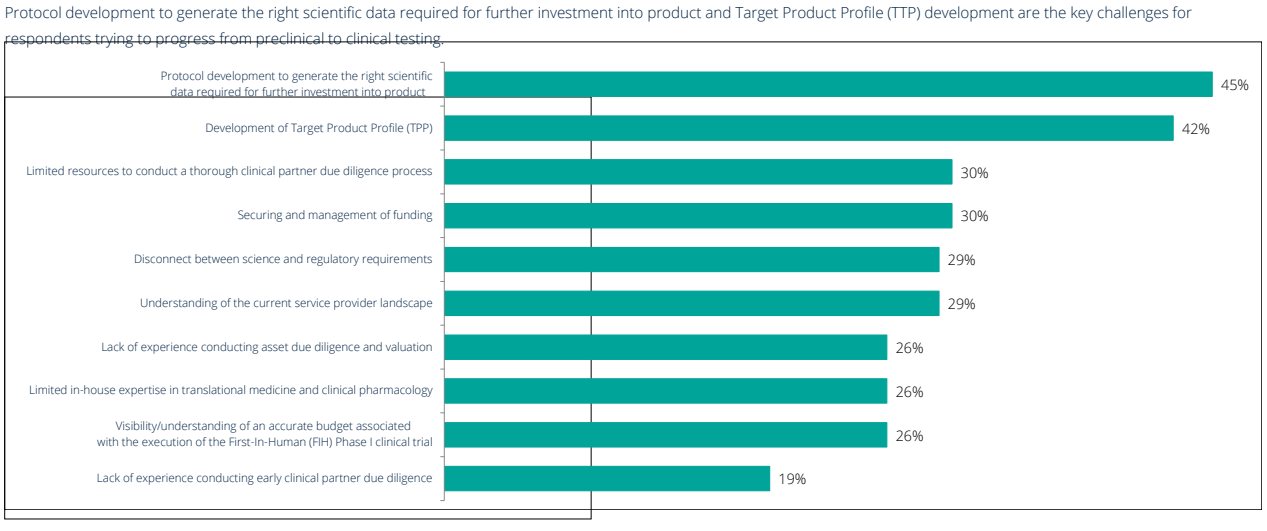
KEY TAKEAWAYS

Survey participants highlighted different challenges at different stages of development.

The survey asked biotech leaders about their most significant challenges in navigating different stages of development.

③ Respondents in the drug development or preclinical stages—with plans to move to clinical testing soon—cited protocol development to generate the right scientific data required for further investment into the product and development of target product profile (TPP) as their greatest challenges.

Figure 1: Key Challenges in Progressing from Preclinical to Clinical Testing



Question: What are your key challenges in progressing from preclinical to clinical testing? (Please select three key challenges)
Base: All respondents; three answers permitted (n=132).

③ Respondents currently engaged in Phase I clinical studies cited navigating compliance and regulatory requirements as their greatest challenge, followed by biomarker selection, participant safety, and protocol uncertainty.

Navigating compliance and regulatory requirements is the main challenge when conducting a Phase I clinical study, followed by biomarker selection and participant safety.

Question: What do you think will be the greatest challenges when conducting your Phase 1 clinical study? (Please select three challenges)
Base: All respondents who are considering partnering with a CRO to conduct your Phase I clinical trial; three answers permitted (n=111).

③ Respondents in the clinical development planning process say their greatest challenges are identification of strategic partnerships for clinical development and protocol development to generate the right scientific data required for further investment into product.

In navigating these challenges, biotechs often prefer to retain core scientific capabilities internally, but perceive great value in forming external relationships for activities they can't do on their own.

A topic on the minds of biotech leaders is constantly thinking about which activities to keep in house and where to enlist outside expertise.

> "It is important for me to always consider what to keep in house and what to contract out."
>
> *Juliane Bernholz, CEO, AM-Pharma*

Internally

The panelists felt strongly about the importance of keeping certain core elements in house. They 'own' the science and therefore see protocol writing, target product profile, and overall asset strategy as something they would keep in house. The preference of these biotech leaders to perform these tasks internally is driven by the view that this scientific and medical work is the core of what companies and insiders need do and that only insiders have the deep asset-level knowledge necessary to develop protocols and TPPs. This is also based on some negative experiences where protocol writing had been outsourced. Whilst these leaders do use external KOLs for some input they see it as unlikely that an outsider will have the same knowledge about a company's science as an insider who lives and breathes the company's science each day.

> "You want to keep science and protocol writing internally . . . we always keep it inside."
>
> *Peter Lichtlen, Chief Medical Officer and Co-founder, Numab Therapeutics*

Externally

However, while these biotech leaders see it as necessary to keep the science in house, they acknowledge that for small biotechs, it is essential to outsource certain tasks. Among the areas where outsourcing or partnering makes sense are:

- Operational support for clinical trials. Small biotechs can't conduct trials on their own; they absolutely must partner for effective trials. Lichtlen said, "For a small biotech, it's impossible to run an international trial. You need the operational hands and the expertise behind them."

  Citeline and ICON's survey supports the idea that partnering with CROs is a necessity, as nearly all survey respondents (97%) consider use of a CRO when formulating their clinical development plan.

> "For early stage trials . . . with a small biotech team, you cannot [run larger trials] on your own. You want to use all the operational expertise that is out there to support you . . . you want to keep the science in house and then have your operational support outside." Key is also for the company to maintain direct contact with the sites, investigators to understand the dynamics and implications of clinical practice."
>
> *Juliane Bernholz, CEO, AM-Pharma*

- Market research. Multiple panelists mentioned the value that external partners can provide to a biotech by conducting vital market research. Bernholz said, "The TPP is central and is something

you should do in house because that's really your strategy and what your label will be, but to gather all of the elements needed in a TPP—like market research, payer research, that's really important to get from outside." In expounding on the market research that is needed, Bernholz mentioned interviews of investigators and of payers. She termed this "a huge logistical effort, which of course needs to be outsourced."

> "I strongly believe the TPP needs to be developed internally. However, I also completely agree that as a small company, certain aspects of market research, payer commitment, etc. you need to outsource."
>
> *Andrea Chicca, CEO and co-founder, Synendos Therapeutics*

③ Commercial analysis. Small, early-stage biotech companies definitely need outside assistance in assessing and analyzing the commercial landscape and the opportunity.

> "The first thing you have to do, before going into your indication, is to decide on your target. In looking for your target, you need to have an understanding of your potential patient number and your competition."
>
> "It is not really a total commercial assessment. But at least you need to understand, 'Is it a niche? Or is it a little broader? Plus, is more coming in the next five years?' . . . These are things we start even before the clinical candidate selection."
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> *Lars Nieba, CEO, Engimmune Therapeutics*

In commenting on the commercial assessment, Andrea Chicca, CEO and co-founder of Synendos Therapeutics, said, "We have to go externally because we cannot do it inside." He added, "Our board requires us to do this; they want to see commercial analysis before they approve huge investments in a clinical trial."

> "Many CROs have consulting groups which specialize in commercial and market positioning. Whilst not all organizations may be adept in conducting NPV analyses they can provide valuable insights into the commercial environment an asset will potentially be operating in. The ability to have scientific, operational, and commercial insights in one organization simplifies vendor management for a biotech company."
>
> *Colin Orford, Senior Vice President Drug Development Services, ICON Biotech*

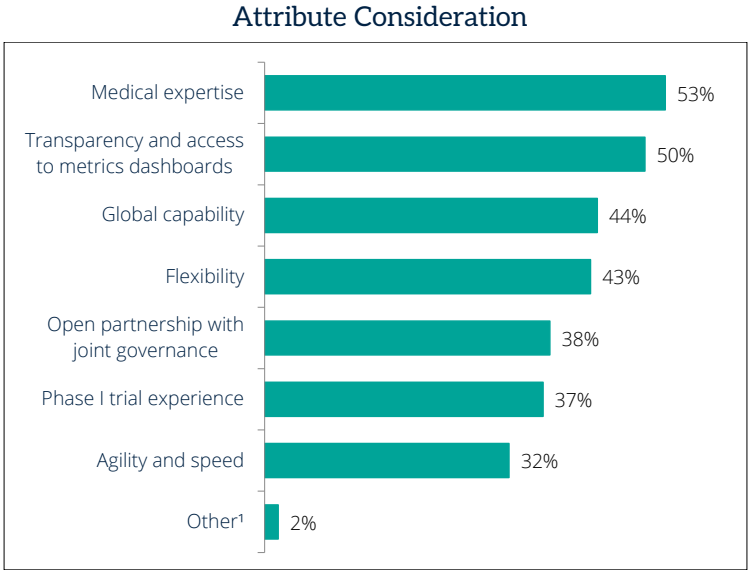
When selecting a CRO, biotechs have several selection criteria.

The survey asked biotech leaders what attributes they look for when considering partnering with a CRO, at different stages of development. Key attributes include medical expertise, transparency, global capability, flexibility, and agility and speed.

Phase I Clinical Trial CRO Partnering Considerations

Respondents in drug development or preclinical stage

84% of respondents are considering partnering with a CRO to conduct Phase I clinical trials



Question: Which of the following attributes do you consider most important when selecting a CRO for Phase I trials? (Please select three attributes) Base: All respondents who are considering partnering with a CRO to conduct your Phase I clinical trial; three answers permitted (n=111). ¹Other: No comments.

For the panelists, when evaluating CROs, operational aspects are obviously important. Lichtlen described how his organization uses a scoring tool that takes into account multiple categories, and that gives each category a different weight; the weights can change, based on the project. Among the factors in this scorecard are the quality of the strategic advice, the governance structure, a CRO's geographic footprint, the team, and the budget.

Key selection considerations mentioned by the panelists include:

- **Quality.** Bernholz mentioned criteria of people, expertise, and cost. In particular, she emphasized, "You choose a CRO that provides you with the best quality. . . to me, the key elements are quality and expertise."
- **Speed of recruiting.** Recruiting and enrolling patients in a clinical trial is a core part of a CRO's role. However, beyond merely recruiting, the panelists see the speed of recruiting as a potential differentiator among CROs. "How fast can you recruit?" asked Lars Nieba, CEO, Engimmune Therapeutics. Bernholz added, "Recruitment is extremely important for biotech companies because time is money." Chicca noted, "It's not just enrollment speed; you also want to make sure you get the patients you need."

- **Medical expertise.** This includes experience in a relevant therapeutic area and/or related to a particular endpoint. Nieba mentioned looking for experience and expertise in trials that used the same modality that his company was considering.
- **Bringing together key opinion leaders (KOLs).** While sponsors have clinical advisors and experts, and engage in their own efforts to build relationships with KOLs, if CROs can do this, that is an added benefit.
- **Governance structure.** From Lichtlen's perspective, governance is extremely important. In thinking about governance, he referred to having access to the CRO's senior management and being able to escalate important issues.
- **The team.** Multiple panelists commented that while the overall CRO is important, even more important is the team that will be working on a particular project. "It's not about selecting the CRO," said Lichtlen. "It's really about selecting the team." Nieba added that it is not merely the capabilities of the team that matters; it is also the communication within the team.
- **Regulatory expertise.** In the Citeline and ICON survey, navigating compliance and regulatory requirements was the number one challenge in Phase I clinical studies. Chicca echoed that challenge, and stressed the importance of a CRO having regulatory expertise. He mentioned a previous experience where a CRO that was naïve about regulatory matters made a mistake that almost caused his company's drug not to be approved, making the addition of regulatory experience a significant factor in selecting a CRO. Nieba agreed, stating, "I would add regulatory expertise as well."

> "We now prioritize regulatory input and expertise [as a selection criterion], particularly in Europe with the new CTIS procedure [regulations] . . . this has become one of our top selection criteria and priorities."
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> *Andrea Chicca, CEO and co-founder, Synendos Therapeutics*

> "All CROs need to understand the detailed regulatory requirements within a region as well as individual countries to support efficient project execution. This should be a core competency. Some CROs can also provide a more comprehensive regulatory service which may include representation with key agencies such as the FDA or EMA."
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> *Colin Orford, Senior Vice President Drug Development Services, ICON Biotech*

Biotech leaders see potential for CROs to provide value in ways that go beyond CROs' traditional value proposition.

Colin Orford, Senior Vice President Drug Development Services, ICON Biotech, observed, "People know that CROs should always be good at delivery. They should always be, because that's what CROs are for." But he asked the other panelists if there were opportunities for CROs to extend the value that they provide.

The panelists shared several comments about ways that CROs can provide additional value.

- **By providing feedback on the protocol.** Nieba said that biotechs typically develop the basic elements of the study protocol internally, with clinical advisors. But, Nieba said, "Getting some feedback, in particular on the operational aspects of the protocol from the CRO, is worthwhile." He pointed out that historically, some biotechs have only involved CROs very late in protocol development, but it could be beneficial to involve CROs earlier.
- **By assessing the "doability" of the protocol and working to optimize it.** Chicca described an experience working with an external partner where the partner took the protocol and discussed it with investigators, study coordinators, and patients—and then provided practical feedback about the protocol. "I think this is something that CROs can do to support protocol development, because I think it's really important to get these different views," he said.

  Orford described how ICON has previously looked at the "doability" of a protocol by taking the proposed schedule of events and reviewing it with the principal investigator, the study coordinator, and patients. The idea is to look at the time burden of various steps across the entire schedule. For example, a step that may sound reasonable to a principal investigator may be viewed as particularly arduous by patients.
- **By providing strategic input.** "We want to hear the strategic thoughts of CROs," said Chicca. Lichtlen mentioned inclusion/exclusion criteria as a particular area where the perspective of an outsider can have significant value.

> "Where I could see more input, especially for young biotechs, is inclusion/exclusion criteria . . . external input might be helpful strategically in helping you think about reaching your final endpoint . . sometimes we think too much only from the inside and not that much from the outside."
>
> *Peter Lichtlen, Chief Medical Officer and Co-founder, Numab Therapeutics*

- **By offering regulatory and compliance expertise.** While multiple panelists mentioned the growing importance of this area of expertise, Lichtlen noted, "The compliance piece is something which is not easy to find." Therefore, those CROs with strengths in this area can differentiate themselves.

> "The core competency of CROs is still very much seen to be associated with operational delivery and execution. However, as CROs evolve and different expertise becomes embedded in these organizations, there is an opportunity for early engagement, pre-RFP, as well as becoming a more integrated partner at the asset rather than study-level. CROs need to become better at promoting this type of expertise and capability to emerging Biotech leaders."
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> *Colin Orford, Senior Vice President Drug Development Services, ICON Biotech*

BIOGRAPHIES

Colin Orford

Senior Vice President Drug Development Services, ICON Biotech

Colin has 33 years of experience in the pharmaceutical sector gained at GSK, Novartis, Quintiles and Eisai which combines development strategy with operational execution. He has over 20 years of hands-on drug development experience in Pharma, having led multiple R&D project teams, and has worked across all stages of the development spectrum from Preclinical through to Phase IIIb. He has led therapy area strategy teams in Alzheimer's, sleep disorders, multiple sclerosis, affective disorders and auto-immune disease. He has been responsible for transitioning multiple molecules, from Preclinical (candidate selection), through proof of concept and, into late phase development. He has also led a number of Phase III teams and has been involved in several NDA and MAA submissions. He retains a strong affiliation with the Neurosciences area. Colin leads ICON's drug development and consulting team, is a member of ICON Biotech senior leadership team. He has developed and established ICON's due diligence capabilities and has continued to focus on developing new models of drug development collaborations which range from fully virtual development, with small companies, through to externalized development approaches for larger pharma. Over the past ten years Colin has developed a strong interest and understanding of the Biotechnology sector having worked extensively with both investors and multiple start-up companies.

Juliane Bernholz

CEO, AM-Pharma

Dr. Juliane Bernholz has over 25 years of experience working in the pharmaceutical and biotech industry in a variety of senior R&D and business development roles. She joined AM-Pharma as Chief Operating Officer in October 2019 where she was responsible for Clinical, Regulatory & Quality and Manufacturing activities. Since September 2023 she assumed the role of CEO.

Prior to joining AM-Pharma Bernholz was a Compound Development Team Leader at Janssen R&D LLC in New Jersey, US, leading projects in Cardiovascular and Infectious Diseases. Before her time at Janssen, Bernholz held a number of international leadership roles in big Pharma and Biotech companies. These included Lead for International Partnering in the Diabetes Division at Sanofi where she successfully executed cell therapy and drug discovery collaboration deal. She also served as Senior Global Program Head of the Critical Care Franchise at Novartis Pharma, where she led work on its Rare Disease Cystic Fibrosis projects. Her prior career included a variety of senior roles at Actelion, Novartis, Ciba and Sandoz.

Bernholz holds a PhD in Cell biology from the Biozentrum of the University of Basel, Switzerland and a Board Director Diploma from the International Institute for Management Development (IMD), Lausanne, Switzerland.

Andrea Chicca

CEO and co-founder, Synendos Therapeutics

Dr. Andrea Chicca holds a Ph.D. in Pharmacology and has over 15 years of professional experience.

Following his initial post-doctoral study, Andrea served as a scientific advisor in the corporate marketing department at Chiesi Pharmaceuticals, gaining valuable hands-on experience in preclinical and clinical drug development.

Afterwards, he transitioned to the University of Bern, joining the research group of Prof. J. Gertsch and progressed to senior scientist and principal investigator. At Bern, he was part of the National Centre of Competence in Research (NCCR) TransCure project aimed at combining basic research and early-stage drug discovery on membrane transporters.

Andrea was appointed as an Adjunct Professor by the Medical Faculty of the University of Bern and completed the Master of Advanced Studies in Translational Medicine and Biomedical Entrepreneurship at Sitem-Insel/University of Bern.

Andrea has co-authored over 50 scientific articles published in international peer-reviewed journals. He has made significant contributions to understanding the endocannabinoid membrane transport mechanism and the development of selective endocannabinoid reuptake inhibitors (SERIs).

Andrea is a co-founder and CEO of Synendos Therapeutics.

Peter Lichtlen

Chief Medical Officer and Co-founder, Numab Therapeutics

Peter is the Chief Medical Officer and a co-founder of Numab. He holds an MD as well as a PhD in Molecular Biology from the University of Zurich. In 2000 Lichtlen joined ESBATech where he led several preclinical and clinical development projects with antibody fragments in oncology, inflammatory and neurodegenerative diseases as the Head of Clinical R&D. In particular, he designed the clinical proof-of-concept trial for brolucizumab/Beovu®, a best-in-class anti-VEGF fragment for the treatment of age-related macular edema, launched by Novartis. In 2011 Lichtlen joined Sucampo Pharmaceuticals, where he became the company's Chief Medical Officer. In this function, he managed the global clinical development portfolio and held overall responsibility for Medical Affairs and Pharmacovigilance and was responsible for interactions with major regulatory agencies as well as HTA bodies, leading to successful NDAs, MAAs and STAs. After the acquisition by Mallinckrodt in 2018, Lichtlen joined Numab as a full-time Chief Medical Officer.

Lars Nieba
CEO, Engimmune Therapeutics

Lars Nieba brings more than 20 years of leadership experience in the development of several pharmaceutical products and innovative technologies. He most recently was CTO and CEO at Nordic Nanovector, a biotech company developing novel radio-immunoconjugates for treating cancers. Previously, Nieba was VP and Strategic Product Lead at Bayer. Before that he held several leadership roles at F. Hoffmann-La Roche in clinical operations, clinical supply planning, biologics technology and business development. Nieba gained his PhD from the Max-Planck-Institute for Biochemistry, Munich, and Institute for Biochemistry at the University of Zurich; he also holds an executive MBA from the University of St. Gallen, Switzerland.

Gerd Arold
Senior Director Scientific Affairs, Clinical Pharmacology, ICON Biotech

Gerd Arold, MD, is expert at early drug development, with over 25 years clinical research experience in early patient trials in pharma and biotech companies and contract research organizations, working globally with medical and scientific experts. Gerd is Senior Director Clinical Pharmacology at ICON Biotech, consulting with project teams and clients on scientific aspects of Study Design and Drug Development.

Gerd is a fully licensed physician and has performed more than 500 studies in close to all therapeutic areas, with a special expertise in clinical pharmacology, first to man, first into patient, as well as studies in special populations. He is a member of the Association for Applied Human Pharmacology, the American Association for the Study of Liver Diseases and of the American Society Clinical Pharmacology Therapeutics and is first author/coauthor in various publications in peer-reviewed journals or book chapters.

Daniel Chancellor
VP of Thought Leadership, Norstella (Moderator)

Daniel Chancellor has over a decade of experience as an analyst in the biopharma industry, spanning roles in drug discovery, market analysis, competitive intelligence, and strategic consulting. He now oversees the thought leadership program for the Norstella companies, Citeline and Evaluate, producing materials that support clients across a range of hot topics in the biopharma industry. As part of this, Chancellor regularly participates in webinars, conferences, and other speaking arrangements, and he has provided expert insights across a wide range of leading industry and business publications. Prior to joining Citeline, Chancellor worked as a medicinal chemist at the UK biotech company Summit Therapeutics and graduated with First Class Honors in Natural Sciences from the University of Bath.