ROUNDTABLE SUMMARY

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Advancements in Oncology: A New Wave of Technology-Driven Therapeutics

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Jerry McMahon, PhD, CEO & President, STORM Therapeutics
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Moderator: Janelle Hart, Managing Editor, Custom Content, Citeline

KEY TAKEAWAYS

- Designing oncologic drugs requires determining the optimal line and combination potential of a therapy, which is often influenced by operational factors.
- Demonstrating monotherapy effectiveness continues to be a major step in oncology, prompting drug developers to strike a balance between incremental change and significant clinical benefit.
- Quality evidence, value, and health equity access considerations are top of mind for life sciences organizations looking to innovate never-before-seen therapies.
- Elevating the importance of operational roles is critical for both small biotechs and large pharma companies.
- Patient diversity is top of mind for sponsors and regulators.
- AI and ML technologies are being applied to bolster clinical research processes and workflows.

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OVERVIEW

As a leading therapeutic area for investment globally, oncology poses numerous opportunities for clinical innovation. From artificial intelligence (AI)-driven drug discovery to CRISPR-based gene editing, the oncology sector is already experiencing a major transformation as life sciences organizations continue to harness the combined power of science and digital technologies. The novel modalities and robust clinical trials that result from this synergy are revolutionizing how efficiently drug developers can deliver cancer treatments to patients.

However, drug development in this space can be arduous, given current oncology-specific challenges that involve improving precision and safety of treatments while reducing the burden on patients. In this ever-changing R&D landscape, it is important to determine when and how technology can be best used to overcome those challenges while keeping innovation top of mind.

CONTEXT

The panelists discussed current and future innovations in oncology, the role that AI and machine learning (ML) can play in improving workflows, and novel approaches to de-risking drug development in this sector.

This conversation took place at the annual conference of the American Society of Clinical Oncology (ASCO), held in Chicago between May 31 and June 4, 2024.

KEY TAKEAWAYS

Designing oncologic drugs requires determining the optimal line and combination potential of a therapy, which is often influenced by operational factors.

The oncology R&D landscape is in the midst of a large-scale transformation, with innovation pushing drug developers to rethink where and how new modalities fit within existing treatment paradigms.

One of the main drivers of this transformation is the idea that drugs typically designed and used as later-line or combination therapies after a first-line therapy has failed may be more beneficial to patients if they were used earlier in the treatment journey. The implication for drug developers is that they will likely have to design drugs differently, anticipating their usage in combination with other drugs upfront rather than independently as later-line therapies.

> "The FDA [supports] maximizing the value of drugs earlier in the lines of therapy, especially in areas of high unmet need where patients don't have much time to be able to afford benefit from certain therapies."
>
> *Ahsan Arozullah, Astellas*

Growing awareness about the potential impact of administering later-line therapies earlier in the treatment journey tracks with efforts to also ensure the patient experience is less onerous. Further, patients who have not been exposed to numerous other treatments prior to receiving a highly targeted second-line therapy may tolerate that therapy better, even if it has a slightly higher risk profile.

> "Some important considerations for patient-centered drug development are that patient's journey through a clinical trial, the number of different steps, treatment cycles, barriers to access, and other kinds of modalities."
>
> *Victoria Chiou, AstraZeneca*

Another trend reshaping oncologic drug development is the recognition that highly targeted modalities that have demonstrated efficacy, such as CAR T-cell therapies, aren't always the route drug developers want to take due to complexity and costs of their manufacturing process, especially when newer modalities are becoming more effective and efficient.

> "The bar for what a CAR-T has to show and the value proposition it would have to establish keeps getting higher and higher."
>
> *Ahsan Arozullah, Astellas*

Despite these considerations, there is an explosion of interest in developing CAR T-cell therapies for the oncology space. Yet, there is also the belief that further innovation may come from recycling old ideas, such as antibody drug conjugates (ADCs) and bispecific antibodies (bABs), which help to combat the patient and financial burden brought on by complex manufacturing requirements.

> "I expect CAR T-cell therapies will have a place in oncology, but big leaps do not only come from the newest modality—sometimes an old idea [such as ADCs] gains a lot more prominence over time as the approach is refined."
>
> *Javad Shahidi, BeiGene*

Demonstrating monotherapy effectiveness continues to be a major step in oncology, prompting drug developers to strike a balance between incremental change and significant clinical benefit.

Regardless of what modality is being developed, it is clear that monotherapy activity must be demonstrated to determine where newer therapies can best fit into standards of care.

Victoria Chiou, MD, head of clinical excellence and innovation at AstraZeneca, who previously served as a medical officer at the FDA, noted the agency assesses data in cancer drug co-development to facilitate risk-benefit assessment and an understanding of the contribution of each individual component used in combination therapies.

Apart from being an FDA requirement, demonstrating monotherapy activity is good practice for life sciences companies because it can serve to justify their initial investment and unlock further levels of investment.

> "It would be too big of an investment risk not to add that data [on monotherapy activity]."
>
> *Jerry McMahon, STORM Therapeutics*

Assessing monotherapy activity is even more critical when an experimental combination therapy is evaluated by using a single-arm study due to the infeasibility of randomizing trial participants to a control group.

Where there is emerging opportunity in oncology R&D to demonstrate monotherapy activity is through neoadjuvant studies and "testing new drugs in therapeutic areas where the technology has progressed so quickly that the current standard of care is based on something that doesn't exist anymore in clinical practice," Ahsan Arozullah, MD, SVP, head of oncology development at Astellas said.

Quality evidence, value, and health equity access considerations are top of mind for life sciences organizations looking to innovate never-before-seen therapies.

Another set of challenges for drug developers includes translating the value of novel therapies to payers, dealing with pricing pressures as successful therapies from a decade ago go generic, and the difficulty of increasing prices for new therapies that end up being phenomenally effective but whose initial price was set at a point below their true value.

Conveying the scientific value of novel therapies to payers can be particularly challenging because often policy lags innovation and demonstrating new relevant endpoints based on new modalities does not fit into existing policies.

Companies may negotiate initial prices if they can demonstrate their therapies are extremely effective in very niche patient populations. "In circumstances where there's a clear unmet need and the value within that population is not just incremental but quite significant, you may be able to get a price higher," noted Arozullah.

> "It's in those calculations where the cost of goods becomes really critical. For CAR-Ts and other 'fancy' therapies that cost a lot more to make, the value proposition has to be much better. If the value that those therapies bring is equivalent or just a little bit better [compared to less costly therapies with similar efficacy], it's probably not going to be good enough to sustain higher prices."
>
> *Jerry McMahon, STORM Therapeutics*

Enabling affordable medicines can also be seen as a success, since it is good from a health equity perspective, as it allows—at least in theory—more patients from low- and middle-income countries to access innovative medicines.

> "We do need to work hard to bring impactful and affordable medicine to more patients around the world with efficient drug development practices. There are big countries where a great majority of the population don't have access to any PD-1 or PDL-1 inhibitor—even today."
>
> *Javad Shahidi, BeiGene*

Elevating the importance of operational roles is critical for both small biotechs and large pharma companies.

While drug development strategy is more fashionable, as Shahidi described, operations excellence should be more focused on in this sector, given the rising competition and increasingly complex protocols in the oncology space.

Selecting experienced trial sites, managing complex logistics, and conducting long-term patient follow-up are all crucial aspects of operations that contribute to the end goal of delivering cancer treatments to patients. Whether it is a small biotech outsourcing to contract research organizations or a large pharma company conducting operations internally, the goal is to increase efficiency and reduce cost.

> "Operations can make or break your study, no matter if you're at a large company or small company."
>
> *Alexandra Snyder, Generate Biomedicines*

Operations is also key for accelerating drug development by setting clear operational and performance targets, leveraging technology, reducing asset spend, and driving efficiency.

> "Reducing spend on a particular asset allows you to develop another asset."
>
> *Ahsan Arozullah, Astellas*

On top of that, operational excellence is ultimately a decisive factor for de-risking. This insight, which was shared by several panelists, runs counter to a common perception that it is regulators who should play more of a role in helping life sciences organizations de-risk asset development. "This is not an FDA or a regulatory issue," Jerry McMahon, CEO & president at STORM Therapeutics, added. "We're being challenged to come up with ways to do this faster, better, and with more potential for a study to reveal interesting activity. That's our job."

Some innovative ways in which companies are improving operational efficiency include using Bayesian approaches to dose escalation, selecting high-risk populations in the adjuvant setting by leveraging circulating tumor DNA technology, and using surrogate endpoints for estimating overall survival. As well, tokenization of patient identities can go a long way toward preventing loss to follow-up in clinical trials, thus increasing the number of data points researchers have to make accurate estimates of overall survival, Arozullah said.

> "Tokenization is very important. We utilize tokenization frequently here in the US, but it is a problem outside because data protection is challenging."
>
> *Andreas Dreps, ICON*

Patient diversity is top of mind for sponsors and regulators.

The life sciences industry is under tremendous pressure to improve patient diversity when researching, developing, and testing new drugs—and the oncology sector is no exception, brought up Andreas Dreps, PhD, SVP, drug development services at ICON.

While drug developers have made efforts to reverse longstanding trends in clinical research, inclusion and exclusion criteria and patient recruitment strategies often involuntarily but effectively discourage minority patients from participating.

> "As an industry, our diversity action plans have primarily been going to sites where diverse patients are and when we don't enroll patients, we go to the FDA and say we weren't able to do so. That's not enough and it's a lousy approach. The fundamental question is why aren't patients enrolling in a trial."
>
> *Ahsan Arozullah, Astellas*

To improve recruitment and enrollment of diverse patients, it is necessary not only to go into diverse communities, but also to ensure that studies are suitably embedded in those communities. This can be achieved by decentralizing trial sites and making it easier to patients to participate remotely, ensuring that physicians' and investigators' ethnicities resemble those of the communities they serve, and even something as simple as ensuring that would-be participants are informed of the opportunity to join a study.

Oftentimes, the main reason why members of diverse populations do not enroll in a trial is because they do not know about it.

> "You have to really put diversity on the table upfront in your drug development strategy and create a diversity action plan, because it will be needed at a later stage."
>
> *Muaiad Kittaneh, ICON*

However, while the goal of improving diversity is readily accepted throughout the industry, the extremely nuanced considerations for patient selection strategy should be taken into account when developing targeted therapies for rare or complex cancers that only affect very specific subgroups of patients. In other words, patient diversity from a demographic, ethnic, or genetic perspective should also be considered alongside diversity from a relevant disease target perspective.

AI and ML technologies are being applied to bolster clinical research processes and workflows.

Advanced AI technologies can support drug development from the earliest stage through trial completion and post-marketing surveillance.

> "If we think of the probability of success of a drug as the probability of choosing the right targets, the probability of making the right drug to go after those targets, and the probability of conducting the right clinical experiment to show convincingly whether that approach worked, AI is being applied to each of those three applications."
>
> *Alexandra Snyder, Generate Biomedicines*

Currently, AI is used most widely to facilitate and accelerate clinical trial operations, such as identifying sites, writing study protocols, translating documents, optimizing patient recruitment, adjusting enrollments, and evaluating site performance. Some also see a potential for applying AI to predict the impact of drugs on patient subgroups, thus improving the odds of maximizing the drugs' efficacy and minimizing their toxicity.

> "AI allows for studying pharmacogenomics early on to predict if a certain ethnic minority may metabolize a certain drug differently than another group of patients where it justifies different dosing schedule or even a different clinical trial design."
>
> *Muaiad Kittaneh, ICON*

When deploying AI to support clinical research operations, however, it is important to make sure the technologies and algorithms are trained on unbiased, diverse datasets. This can be challenging for organizations because so many pharma datasets today contain data that may have been collected from older studies, when diversity was not yet a top priority.

> "It's really an important consideration to develop principles for ethical data and AI to reduce bias in AI."
>
> *Victoria Chiou, AstraZeneca*

CONCLUSION

The oncology R&D space is undergoing tectonic shifts in how research is being planned, conducted, and made more efficient with the help of advanced technologies such as AI and ML. As the adoption of these technologies increases, both small biotechs and large pharma companies see an opportunity to rethink and reinvent many of the processes they have traditionally used.

Given the pace of technological innovation and adoption, the outlook for the industry is optimistic. By strategically reconceptualizing R&D, focusing on operational and patient-focused improvements, and working in close collaboration with regulators, drug developers in oncology have vast opportunities to transform the sector by leveraging AI and ML, while delivering more precise and actionable data. It is in their hands to make the most of those opportunities and steer the course of innovation.

ASCO, the forum at which this conversation took place, itself speaks to this trend. "You see it in the poster sessions, which would have been presented on a podium a couple years ago," Arozullah said. "Phase 2 and 3 studies are all [presented as] posters now because of the rapidity and quality of the work we're doing."

BIOGRAPHIES

Ahsan Arozullah, MD

SVP, Head of Oncology Development, Astellas

Ahsan M. Arozullah, MD, MPH, is currently Senior Vice President, Head of Oncology Development at Astellas. Arozullah has over 20 years of clinical research experience in the pharmaceutical industry and academic settings. His passion for delivering lifesaving and life-changing therapies for patients is founded from his personal losses of loved ones to cancer. He leads a global team of Asset Leads and Medical Directors who provide world-class leadership to clinical development teams dedicated to creating the next generation of targeted oncology therapies. By actively collaborating globally with top scientists, clinicians, and caretakers, Arozullah leads his team in developing novel therapies in patient-centric ways that facilitate Astellas' collective aim to bring the highest life-changing value to patients.

Victoria Chiou, MD

Head of Clinical Excellence and Innovation, AstraZeneca

Victoria L. Chiou, MD, is Head, Clinical Excellence and Innovation, Late Development Oncology at AstraZeneca, where she leads strategic development and implementation of global initiatives at the intersection of clinical cancer research, technology, and innovation. Chiou is an oncology research physician with academic, industry, and regulatory experience in patient-centric drug development. Prior diverse clinical development experiences include GlaxoSmithKline in cell therapy, and MedImmune/AstraZeneca in novel immuno-oncology drug combinations for treatment of multiple cancers. Chiou also served as a medical officer at the US Food and Drug Administration, Office of Hematology and Oncology products.

Chiou completed her BA in human biology and psychology as a Jefferson Scholar at University of Virginia, MD at Medical College of Virginia, internal medicine residency at Wake Forest University, and medical oncology fellowship at National Institutes of Health, National Cancer Institute. Multiple career recognitions include Conquer Cancer Foundation of ASCO Merit Award, ASCO/AACR Methods in Clinical Cancer Research Workshop, and SITC Women in Cancer Immunotherapy Network Leadership Institute. The statements expressed at the Roundtable are Chiou's personal opinions and not associated with her affiliation with any current or former organization.

Andreas Dreps, PhD

Senior Vice President, Drug Development Services, ICON

Andreas Dreps has over 25 years' experience in clinical research and development in a variety of solid tumours and haematology diseases. Prior to joining ICON, Dreps held positions at BMS, Aventis Medical, and Merck/Serono, where he was involved in the development of paclitaxel, docetaxel and Erbitux. At ICON Dreps heads the Oncology Drug Development Services group, where he is accountable for the provision of a fully integrated, scientific and strategic development service to ICON's oncology customers. This service includes scientific, technical and therapeutic strategic expertise that spans the full development cycle from gap analysis of the pre-clinical data, development of a TTP, providing scientific lead with regards to interactions with regulatory authorities, developing FIH study concepts, through POC, pivotal trial designs, market authorization applications to post approval activities, applicable to all types of new oncology drugs, combination therapies and diagnostics. During his career he was involved in 35 oncology IND applications that finally led to market authorizations for more than 10 new oncology drugs.

Muaiad Kittaneh, MD, MBA, FACP

Senior Director, Oncology Drug Development, ICON

Muaiad Kittaneh has more than 15 years of medical practice experience, including 11 years in the field of Hematology and Medical Oncology. He was an Assistant Professor of Medicine in the Department of Experimental Therapeutics at Karmanos Cancer Institute and an Associate Professor and completed a master's degree in health care business administration at Loyola University. He served as a Principal Investigator and Co-Investigator on numerous phase I through phase III clinical trials and co-authored several publications in peer-reviewed medical journals and was an invited speaker at multiple national and international scientific meetings. Kittaneh earned his Medical Degree from Al-Quds University, completed internal medicine residency training at Advocate Christ Medical Center/UIC and fellowship at the University of Miami Sylvester Comprehensive Cancer Center and Jackson Memorial Hospital.

Jerry McMahon, PhD

CEO & President, STORM Therapeutics

Jerry McMahon has over 30 years of biotechnology leadership, scientific innovation, creative deal-making, and financing experience. With broad disease-area expertise and a specialty in oncology therapeutics, McMahon has held scientific, pharmaceutical and venture capital positions and has been the CEO or President of multiple biotechnology companies leading novel therapeutic programs from discovery, development to drug approvals for internal and in-licensed products.

From 2016 to late 2021 McMahon was President and CEO of NASDAQ listed Harpoon Therapeutics building the Company from early stage through to IPO, follow-on financings, and development collaborations. Prior to that he held multiple positions, including President and CEO of Kolltan Pharmaceuticals which was acquired by Celldex, Innovative Medicine Head of Oncology and SVP at AstraZeneca-Medimmune, managing a more than $1 billion global R&D budget and President at SUGEN/Pfizer where he was instrumental in invention and full development of several ground-breaking protein kinase inhibitors including sunitinib (Sutent®).

McMahon has also held academic appointments at the Yale Comprehensive Cancer Center at Yale University, Tufts University School of Medicine, and the Massachusetts Institute of Technology. He received his BS in biology and PhD in the field of biochemistry and genetics from Rensselaer Polytechnic Institute, has authored over 100 scientific and medical publications and is an inventor on over 60 US patents.

Javad Shahidi, MD

SVP, Head of Biotech Unit, BeiGene

Javad Shahidi, MD, MSc, is currently Senior Vice President and Head of Biotech Unit at BeiGene, creating an innovative development ecosystem to foster efficiency, focus, and streamlined decision-making. Over the past two decades, Shahidi's career has been dedicated to cancer research in both academia and industry. He has held increasing responsibilities in oncology clinical development and has led the clinical development and regulatory submissions of multiple compounds leading to their global approvals across several indications.

Alexandra Snyder, MD

EVP, Head of R&D, Generate Biomedicines

Alex Snyder is the Head of Research and Development at Generate Biomedicines, a biotechnology company that uses generative AI together with machine learning and protein engineering to create novel medicines. Prior to joining Generate in 2022, Snyder was a Principal at the biotech incubator Two River, following her role as Associate Vice President and Head of Translational Oncology at Merck. She previously was Translational Medicine Lead at Adaptive Biotechnologies, and started her career as faculty and federally-funded Principal Investigator at Memorial Sloan Kettering Cancer Center. She is a Clinical Assistant Professor of Medicine at NYU and Bellevue Hospitals, Section Editor for the Journal for the Immunotherapy of Cancer, and a member of the board of Navigating Cancer.

Snyder received her medical degree and internal medicine training at the Icahn School of Medicine at Mount Sinai and Mount Sinai Hospital, followed by medical oncology fellowship at Memorial Sloan Kettering Cancer Center (MSKCC).

Janelle Hart

Managing Editor, Custom Content, Citeline (Moderator)

Janelle is an experienced writer and editor with a background in health care communications and journalism. She currently produces custom content across an array of mediums and platforms that focuses on pharmaceutical and biotechnology news and insights. In addition, she contributes to Citeline's flagship content, such as Scrip Asia 100, Outlook and *In Vivo's* Rising Leaders series. Janelle received a dual bachelor's degree in English and Media and Culture from Miami University and is currently pursuing a master's degree in Publishing and Writing from Emerson College in Boston, where she currently resides.