ROUNDTABLE SUMMARY

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Industry News & Insights

# Next-Generation Immunotherapy for Solid Tumors: Breaking Through Resistance with Engineered Immune Therapies

**Presenters:**
**Brian Abbott, MD,** Executive Director of Medial Affairs, Allucent
**Haifeng Chen, PhD,** Chief Executive Officer, Virovek, Inc.
**Reagan Jarvis,** Chief Executive Officer & Co-Founder, Anocca
**Lawrence Lamb,** Executive Vice President & Chief Scientific Officer, IN8bio, Inc.
**Geraldine Paulus,** Co-Founder & Vice President of Corporate Development and Operations, Crossbow Therapeutics

**Moderator: Meredith Landry,** Managing Editor, Custom Content, Citeline

## KEY TAKEAWAYS

- Immunotherapy successes in hematologic cancers have yet to be replicated in solid tumors
- Biotech companies are pursuing innovations in immune targeting
- Combination strategies will be key to advancing effective immunotherapy for solid tumors
- Solid tumor immunotherapy development can draw on key lessons from hematologic trials
- Biotechs are reducing trial risk through safety-focused dosing and execution strategies
- Regulators are receptive to collaboration, and early engagement is essential
- Some key success factors for advancing next-generation immunotherapies include targets, scale, and CRO support

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## OVERVIEW

Immunotherapy has reshaped cancer care: Checkpoint inhibitors have produced durable responses in several solid tumors, while engineered immune therapies, most notably CAR T-cell treatments, have achieved significant outcomes in multiple hematologic malignancies. Replicating the success of engineered immune therapies in solid tumors has proven far more challenging, given barriers such as the tumor microenvironment, antigen selection, and safety constraints.

Building on the hematologic successes, researchers are advancing a new wave of next-generation engineered approaches for solid tumors, including engineered T-cell therapies (e.g., CAR T, TCR-T), bispecific antibodies, and other targeted immune engagers, designed to overcome these obstacles.

## PURPOSE AND SCOPE

In a recent roundtable hosted by Citeline, scientific leaders from early-stage immunotherapy companies and a global CRO came together to discuss the advancement and future potential of engineered immune therapies for solid tumors. The conversation examined what's working now, what still stands in the way, and how these innovations could reshape treatment. Topics included lessons from hematologic oncology trials, innovative trial designs to reduce risk, strategies for combination therapies, regulatory engagement, and scalability.

Collectively, these insights offer a forward-looking perspective of how next-generation engineered immune therapies could overcome the barriers that have limited immunotherapy's success in solid tumors.

## KEY TAKEAWAYS

### Immunotherapy successes in hematologic cancers have yet to be replicated in solid tumors

While CAR T-cell therapy has revolutionized immunotherapy treatments for certain hematologic malignancies, translating that success to solid tumors has been far more challenging.

Many promising approaches have shown strong activity in preclinical models but have failed to replicate those results in human trials, in part because animal models cannot fully mimic the complexity of human tumors and immune responses. Solid tumors such as glioblastoma, ovarian cancer, colorectal cancer, and small cell lung cancer present unique obstacles, including an immunosuppressive tumor microenvironment, antigen heterogeneity, and limited immune cell infiltration. Even when tumor shrinkage has been achieved, these responses have not consistently translated into improved overall survival.

> "The solid tumor world is going to require a lot more work with the CAR T system. I think one of the issues you run into is that a lot of funding for CAR Ts early on was based on response before the extent (or lack thereof) of durability was known. The field raised a lot of money showing that you can make a big tumor a little tumor—but when the patients still died on time, large portions of the industry died shortly thereafter."
>
> *– Lawrence Lamb, IN8bio*

Several panelists noted that one of the most significant challenges hindering progress in immunotherapy for solid tumors is the difficulty of identifying truly tumor-specific targets. Reagan Jarvis, CEO and co-founder of Anocca, said, "The solid tumor space is a target problem, not a T-cell problem."

> "It's challenging to identify tumor-specific targets, especially in the solid tumor space, such that you're not targeting normal tissue."
>
> *– Geraldine Paulus, Crossbow Therapeutics*

### Biotech companies are pursuing innovations in immune targeting

To address these challenges and advance immunotherapy for solid tumors, biotechs are pursuing a range of innovative approaches and strategies, which include TCR-T (T-cell receptor-engineered T cells), gamma delta T cells, bispecific antibodies, and more. Among the approaches mentioned were:

- **TCR-T cell therapies.** Anocca is developing TCR-T therapies using a proprietary platform that maps and characterizes HLA-peptide targets. Once identified, these targets are then used to engineer T cells with tumor-specific T-cell receptors for solid tumor indications. "We're using T-cell receptors for reprogramming at the stage of target cells," said Jarvis, noting that Anocca's first program with internal TCR-T manufacturing capabilities is now heading to the clinic. "Engineered cell therapies are always going to be more potent for these low-density HLA peptide targets," Jarvis added.

- **Gamma delta T cells.** IN8bio is advancing gamma delta T-cell therapies that leverage innate immune function and genetic engineering to target solid tumors. These cells recognize stress-induced antigens independently of HLA, providing unique advantages in targeting solid tumors. One innovation is a non-signaling CAR that directs the cells to the tumor without triggering activation—allowing the cell's natural cytotoxic response to destroy the tumor. In broader terms, Lawrence Lamb, executive vice president and chief scientific officer, IN8bio, Inc., said, "I think moving forward, we really need to have new [immunotherapy] ideas to be able to deal with systemic disseminated solid tumors."
- **Bispecific antibodies.** Crossbow Therapeutics is advancing TCR-mimetic bispecific antibodies designed to recognize intracellular targets with the precision of T cells, while maintaining the scalability and manufacturability of antibodies. This approach provides "the ability to select more tumor-selective and prevalent targets from the entire universe of cancer antigens, rather than from the more limited pool of surface proteins, a key challenge right now in the solid tumor space," said Geraldine Paulus, co-founder and vice president, Crossbow Therapeutics. By focusing on targets that are both tumor-specific and highly prevalent within each indication, Crossbow aims to overcome some of the key limitations in current solid tumor immunotherapy strategies.

## Combination strategies will be key to advancing effective immunotherapy for solid tumors

In addition to the innovative approaches discussed above, the panelists agreed that novel cell-based immunotherapies, such as CAR T and other engineered T-cell approaches, are most likely to achieve their greatest potential for lasting remissions—and, in some cases, cures—for solid tumors when used in combination with adjunctive treatments.

"You're probably not going to produce lasting remissions from solid tumors with a CAR T monotherapy, but you can probably produce these lasting remissions, even cures, with a CAR T or other cell therapy and some adjuvant combination therapies," said Lamb. "We have to work together to bring cures to patients because I don't think one shot is going to do it."

Lamb added that when treating patients, providing induction therapy and consolidation therapy, and then coming with immunotherapy, offers a much better chance of success than waiting for the tumor to come back and then trying to treat it.

> "It's unreasonable to expect CAR Ts to work by themselves and clear big tumor masses in solid tumor settings. It is really about combos in smart ways."
>
> *– Reagan Jarvis, Anocca*

Paulus supports pursuing combination strategies but emphasized taking a step-by-step approach. "You want to walk before you run; start with one program and then combine later on," she said.

The panelists emphasized the importance of using these novel immunotherapies and their combination regimens earlier in the course of treatment rather than waiting until other options have proven ineffective.

One panelist from the viral vector manufacturing field offered an additional perspective, noting opportunities for localized delivery using engineered AAVs. While still in early development, this approach illustrates the breadth of strategies being explored across the immunotherapy landscape.

## Solid tumor immunotherapy development can draw on key lessons from hematologic trials

Successful hematologic trials offer valuable lessons for the clinical development of immunotherapies for solid tumors, particularly in ensuring rigorous trial design, clearly defined indications and patient populations, and the use of quantitative dose modeling.

Jarvis attributed the success of first-generation CAR T products to excellent trial design and execution, along with successful trials focused on specific subsets of B-cell malignancies. He contrasted this approach with a long history of "big basket trials," which were noisy, time consuming, and spread across multiple indications. He cited the key lesson as focus.

> "The lesson that we've taken for developing our programs [of immunotherapies for solid tumors] is to make them focused, make them targeted. They are precision therapies so let's do precision trials with pathways to approvable products."
>
> *– Reagan Jarvis, Anocca*

A lesson that Paulus drew from trials in the hematologic space was the use of Quantitative Systems Pharmacology (QSP) modeling to determine the starting dose for Phase I trials. She said, "We used this approach for our first program, CBX-250, a novel T-cell engager for myeloid malignancies, and we have another solid tumor program where we'll aim to use the same approach."

## Biotechs are reducing trial risk through safety-focused dosing and execution strategies

In addition to advancing the immunotherapy development pipeline, biotechs are prioritizing strategies to reduce trial risk.

One area of focus is cytokine release syndrome (CRS), a serious immune system reaction associated with CAR T and bispecific therapies. To address the risks of CRS, immunotherapy developers are adapting trial designs to mitigate potential adverse effects. One strategy to reduce risk is changing the administration of T-cell engagers from intravenous to subcutaneous delivery. This method maintains the same overall drug exposure but slows its release, reducing peak drug concentrations in the bloodstream, helping to limit cytokine release.

A second strategy is step-up dosing, which gradually increases to the target dose to allow the patient's immune system to adapt to the heightened immune activity from T-cell engagers. Another strategy is the use of sentinel dosing, in which the initial dose is given to one or two patients who are closely monitored for adverse effects before treating the rest of the patient cohort.

> "From a CRO perspective, across multiple programs, we're seeing studies [involving immunotherapies] with staggered dosing, other forms of dose ramp-up, and use of sentinel patients."
>
> *– Brian Abbott, Allucent*

## Regulators are receptive to collaboration, and early engagement is essential

Panelists emphasized that regulators are increasingly open to collaboration in oncology immunotherapy development, and early, substantive dialogue can materially shape program strategy by aligning trial design, endpoints, and potential expedited pathways. In the US, the current FDA leadership appears to be prioritizing oncology therapies with meaningful, durable benefits, such as extended survival or potential cures, rather than approvals based solely on short-term tumor response. In Europe, regulators have been supportive of early-stage biotechs developing immunotherapies, and are often willing to engage in early, constructive dialogue. The overarching message for biotechs developing next-generation immunotherapies is to be proactive and engage with regulators in key markets early in development.

> "We've had quite a positive experience with the FDA; the agency is coming around on some alternative dosing paradigms. I would advise people to start engaging with the agency early on. It was very helpful to start a dialogue early; they ended up being very supportive."
>
> *– Geraldine Paulus, Crossbow Therapeutics*

## Some key success factors for advancing next-generation immunotherapies include targets, scale, and CRO support

The panelists identified several critical success factors for advancing next-gen immunotherapies for solid tumors from pre-clinical through pivotal trials: strong targets, the ability to scale manufacturing, and access to expert CRO support.

### *Targets*

Reiterating the theme of highly-focused trials, the panelists agreed that one of the most important factors in advancing immunotherapies for solid tumors is "good targets." For next-generation approaches, this means finding antigens that are both highly prevalent in the intended cancer type and absent from healthy tissue to minimize off-tumor toxicity. In solid tumors, this challenge is amplified by antigen heterogeneity and the presence of shared antigens with normal cells. Selecting truly tumor-specific targets can improve safety, enhance treatment efficacy, and streamline regulatory review.

### *Scale*

Jarvis termed CAR T as a "cottage industry." He estimated that last year, worldwide, there were perhaps only 15,000 to 20,000 doses of CAR T therapies. This low number of doses is due in part to the extremely high cost per dose, which can be hundreds of thousands of dollars or more.

A critical success factor for all immunotherapies, especially those for solid tumors, is greater volume and scale, which will result in lower costs. Together, greater scale and lower costs will help expand the use of immunotherapies for solid tumors.

### *CRO support*

For biotechs, another critical success factor is partnering with experts who can help navigate the strategic, regulatory, and clinical development process. A CRO like Allucent offers the capabilities and experience to support sponsors through this complex process from start to finish.

> "We get to work with a lot of sponsors, and it can be a very productive partnership. We can assist with understanding the science, consulting on the regulatory aspects and helping prepare for early regulatory meetings, pharmacology, running quantitative modeling for dosing, and then executing your trial."
>
> *– Brian Abbott, Allucent*

## CONCLUSION

CAR T-cell therapies have been a life-saving breakthrough for some blood cancers, but multiple obstacles have prevented the development of effective immunotherapies for solid tumors, including the tumor microenvironment, antigen heterogeneity, and limited immune cell infiltration. However, there is growing optimism about next-generation immunotherapy development for solid tumors, with much of the innovation coming from small biotech companies. This work holds great promise, with advances in areas such as TCR-T therapies, gamma delta T-cell platforms, TCR-mimetic antibodies, and more.

Next-generation immunotherapy developers are learning from the past, applying lessons from successful immunotherapy trials in hematologic malignancies, including precise patient selection, rigorous trial execution, and narrowly defined targets. They are updating the playbook: advancing combination strategies that integrate next-gen immunotherapies with clinically established modalities, moving promising therapies earlier in the treatment timeline, and using strategies such as step-up or sentinel dosing to reduce safety risks. Success will also depend on proactively engaging with regulators early in key markets, expanding scale to drive down costs, and partnering with expert CROs who can help navigate this complex process—from early development planning through trial execution, and regulatory approval.

By blending proven lessons from the past with innovative advancements in next-generation immunotherapies, these efforts offer renewed hope for delivering more effective durable treatment and ultimately better outcomes for patients.

# BIOGRAPHIES



## Brian Abbott, MD

Executive Director of Medial Affairs
Allucent

Dr. Brian Abbott is a medical professional with over 25 years of experience in hematology oncology, including thirteen years in the biomedical research industry. As the Executive Medical Director and Therapeutic Area Medical Lead for Oncology at Allucent, Dr. Abbott oversees clinical trial strategies and medical monitoring for hematology/oncology trials and leads the global oncology medical team at Allucent. His career includes senior medical leadership roles at Myriad Genetics, Caris Life Sciences, and Color Genomics.

Prior to his industry roles, he spent a decade in clinical practice as faculty at three NCCN member institutions, focusing on leukemia, lymphoma, and bone marrow transplantation (BMT), while serving as a principal investigator in numerous oncology studies. Dr. Abbott's expertise spans CAR T studies in prostate and hepatocellular cancers, TKIs across various indications, bi-specific antibodies, cytotoxic chemotherapy, and vaccine/cellular therapies. He has significant experience with companion diagnostics registration and phase 1 clinical trials.

Dr. Abbott earned his M.D. from the University of Tennessee, an MBA from the University of Colorado, and a master's degree in finance from the University of Wisconsin. He is board-certified in Hematology/Oncology, Pediatrics, and Hospice/Palliative Medicine.



## Haifeng Chen, PhD

Chief Executive Officer
Virovek, Inc.

Dr. Haifeng Chen is a globally recognized pioneer in gene therapy, with over three decades of transformative contributions to adeno-associated virus (AAV) technology and biopharmaceutical innovation. He earned his B.S. in Biology from Sun Yat-sen University (1982), M.S. in Biology from Sichuan University (1985), and Ph.D. from the University of Saarland, Germany (1992). In 1992, he received the prestigious Marion-Merrell-Dow Post-Doctoral Fellowship, conducting groundbreaking research at the University of Kansas Medical Center.

Chen's distinguished career includes leadership roles at leading gene therapy companies, including Cell Genesys, Genovo, Avigen, and Asklepios BioPharmaceutical. In 2006, he co-founded Virovek, serving as Chief Executive Officer until 2019. There, he invented the revolutionary "BAC-to-AAV" system, utilizing baculovirus and Sf9 cells to achieve 10–100x higher AAV yields than traditional plasmid transfection methods, setting a new standard for scalable, high-potency AAV production.

In 2019, Chen co-founded Avirmax, Inc., where he served as Chief Technology Officer and Chief Operating Officer until 2022. Returning to Virovek in August 2022 as Chief Scientific Officer and Vice President, he continues to drive cutting-edge advancements. In 2024, he developed the innovative PACE (Precision AAV Capsid Engineering) technology, enabling precise AAV capsid modifications to target specific cell types based on surface markers. This breakthrough has propelled Virovek to the forefront of in vivo CAR T therapy and solid tumor immunotherapy, with its AAV-based in vivo CAR T therapy yielding successful preclinical data and advancing toward an IND filing by the end of 2025.

A respected figure in the scientific community, Chen has served on the Viral Gene Transfer Vector Committee of the American Society of Gene and Cell Therapy (ASGCT) and the editorial board of *Molecular Therapy – Methods and Clinical Development*. His visionary leadership and relentless pursuit of innovation continue to shape the future of gene and cell therapy, addressing critical unmet medical needs with transformative solutions.



### Reagan Jarvis

Chief Executive Officer & Co-Founder
Anocca

Reagan Jarvis is the co-founder and CEO of Anocca, a T-cell immunotherapy company based out of Sweden, commencing FIH clinical trials in 2025 with TCR-T cell therapy products in oncology.

A New Zealander, Jarvis obtained his PhD in Biochemistry at University of Otago and performed postdoctoral research at the University of Otago and thereafter the German Cancer Research Center (DKFZ) in Heidelberg. He founded Anocca with Mikael Blomqvist in 2014.

Anocca currently has a pipeline of 40 products. It has 120+ staff, with 36 nationalities and operates the largest cGMP cell therapy manufacturing site in the Nordics.



### Lawrence Lamb

Executive Vice President & Chief Scientific Officer
IN8bio, Inc.

Dr. Lawrence Lamb leads scientific and translational strategy as scientific co-founder, Executive Vice President, and Chief Scientific Officer of IN8Bio. While originally extending his NP clinical training in cardiovascular disease as a PhD student, he switched gears and studied immunology, finishing his PhD with a concentration in inflammatory lung disease and macrophage biology followed by postdoctoral training in molecular evolution and genetic engineering of mouse embryonic stem cells to define gene function. During a second postdoc in transplantation immunology at the South Carolina Cancer Center he was the first to describe the association between relapse-free survival and homeostatic γδT cell recovery in high-risk leukemia patients. While continuing this work as an Associate Professor and later Professor of Medicine at the University of Alabama at Birmingham, Lamb developed the scientific support for chemotherapy resistant γδT cell-based immunotherapy for high-grade brain tumors. This work eventually culminated in successful IND applications that lead to the formation of IN8Bio. Over the course of his career, Lamb's work has been funded by adiverse array of government and the NCI, NHLBI, NCRR, NINDS, the Children's Oncology Group, the Elsa Pardee Foundation, the Leukemia and Lymphoma Society, and the National Brain Tumor Foundation including the Samuel Gerson Leadership Chair for Glioblastoma Research.



### Geraldine Paulus

Co-Founder & Vice President
Crossbow Therapeutics

Geraldine Paulus co-founded Crossbow Therapeutics in October 2021, while a member of the investment team at MPM Capital (now MPM BioImpact), and has served as Crossbow's Vice President of Corporate Development and Operations since July 2022. Paulus brings a decade of cross-disciplinary and translational academic experience and spent four years in Venture Capital (The Engine, MPM BioImpact), where she focused on due diligence, business development, and company creation.

Paulus holds B.S. and M.S. degrees in Chemical Engineering from the KU Leuven (Belgium), a Ph.D. in Chemical Engineering from the Massachusetts Institute of Technology (MIT) and was a postdoctoral fellow in Dr. Ramnik Xavier's lab at Mass General Hospital (MGH) and The Broad Institute.



### Meredith Landry (Moderator)

Managing Editor, Custom Content
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Meredith Landry is the Managing Editor of Custom Content at Norstella. She is a seasoned writer, editor, content strategist and moderator. With a career spanning digital media, print publications and live events, she has built a reputation for elevating content strategies and fostering meaningful discussions. Landry has led editorial teams, developed content strategies and produced high-quality publications for major organizations in industries including healthcare, geospatial intelligence, real estate and more. She has managed newsroom operations, produced live and recorded podcasts and served as a conference moderator. Landry has a journalism degree from Loyola University New Orleans and currently lives in Los Angeles, California.