Lumanity | Cancer Progress 2026

Beyond Next-Gen

How We Engineer Future Breakthroughs

Cancer Progress 2026 Panel Recap
Defining “breakthrough” as patient impact, then designing proof that holds up under scrutiny



“Next-gen” and “breakthrough” are easy words to say. The hard part is delivering a step-change that matters to patients and building a proof pathway that can survive modern constraints long enough to get them there.

Dennis Chang set the definition early and kept the room anchored to it:

“When we’re talking about breakthroughs, all we’re really talking about is innovation that provides transformative benefit to patients. It’s not innovation for innovation’s sake. It’s something that really moves the needle.”

Cancer Progress brings **35+ years** of scientific discussions and connections.

Meet the panel



MODERATOR

Dennis Chang

Strategy Consulting, Lumanity



Joe Guidi, PhD

VP, Worldwide Head of Immunology, Medical Affairs, Bristol Myers Squibb



Alicia Zhou, PhD

CEO, Cancer Research Institute



Zhen Su, MD MBA

CEO, Marengo Therapeutics



Axel Hoos, MD, PhD

Founder & CEO, Argonaut Bio

Setting the Bar: What Defines a Breakthrough?

Axel Hoos reinforced the point and pushed the discussion away from “new target versus old target” debates and toward a more practical lens.

He used HER2 to illustrate the point: **“HER2, 1998, was Herceptin’s approval. 2022 was Enhertu’s approval. That’s the same antibody, just with a new conjugate. Enhertu has a hazard ratio of 0.4 over the previous ADC, so the point is biology matters here. The tools we have, have gotten better over time.”**

The takeaway is that “next-gen” only matters if it changes response rates, durability, and/or tolerability sufficiently to be meaningful to patients. Similarly, novel targets and novel modalities can only be considered breakthroughs if they unlock substantially better outcomes for patients. However, breakthroughs can be reached through a series of incremental steps; it won’t always happen in one giant leap. Various research strategies may be taken to try to achieve a breakthrough; the key is to keep that ultimate goal in mind, make the delta requirement explicit early, and invest continuously toward transformative outcomes, not settling for the intermediate increments.

However, the panel recognized why this is hard. Breakthroughs are possible, but only when treatment strategies are well matched to the disease biology. And the biology is complex, heterogeneous, and often poorly understood. Most cancers remain high-unmet-need diseases where progress is slow or has stalled, and it is often because we pursue the wrong strategies for the biology. Because the biology remains largely a black box. That's the core challenge for our industry: how do we engineer transformative outcomes when the uncertainty is structural?



Spaghetti Against the Wall and the Need to Go Beyond It

The answer, in part, is to start by "throwing spaghetti against the wall and seeing what sticks," and as Chang noted, the field has produced breakthroughs this way. When the biology is mysterious, experimentation may be the fastest way to make progress. Zhen Su made the pragmatic point memorable: **"Spaghetti is good, it feeds the family."**

At the same time, the panel acknowledged that it can't be the only strategy. Broad experimentation can be used to generate leads and insights, and from there decisions with clear criteria for next steps. However, it is extremely resource-intensive.

As Joe Guidi pointed out, this is especially problematic when developing combination regimens. When teams mix and match broadly, the number of permutations explodes: **"What ends up happening then is that the dimensionality of spaghetti that you can throw becomes vast, which means that the amount of money you can waste becomes enormous."**

In short, if you are going to explore, you need to define the conditions under which exploration is justified, and the conditions under which you narrow or stop. Which means you need the governance processes and expertise and wisdom to make those decisions. Without those guardrails, exploration does not de-risk a program. It increases uncertainty and consumes runway.

System-level Challenges Requiring System-level Change

Su called out today's funding reality as one obvious constraint. He pointed out that early datasets behind historical breakthroughs may not be fundable in the current environment. **"If you look at the initial KEYNOTE-001 datasets, it's crappy; I don't think if you take that data sets today you can raise any funding from the investors."**

At the same time, as Alicia Zhou pointed out, building a commercial case is becoming more challenging as we build more targeted therapies that work better in smaller populations: **"The reality is that that actually reduces the TAM [total addressable market] of your molecule."**

In parallel, the cost and structure of Phase 1 through Phase 3 have not shrunk at the same rate. Su described the mismatch in blunt terms: **"Talk about a billion dollars to develop one compound, with a failure rate of 97%. We're still living in the old business model, from phase 1 to phase 2, and from phase 2 to phase 3."**

How do we address these system-level problems? Chang raised the need for system-level solutions. If the field moves toward more precise combinations, can the regulatory approval process adapt to include mechanisms like imputation, so teams are not required to empirically re-demonstrate everything in the same way, every time, in shrinking populations?

Of course, development and commercialization leaders in biopharma cannot simply wait or advocate for systems to evolve. We need to continue to strive for future breakthroughs and design proof pathways that move the field forward and can partially overcome the limitations of our flawed system. And in doing so, perhaps push systems to adapt in turn. The big question is how?

AI/ML Can Move Us Forward, if Biologically Anchored and Well Governed

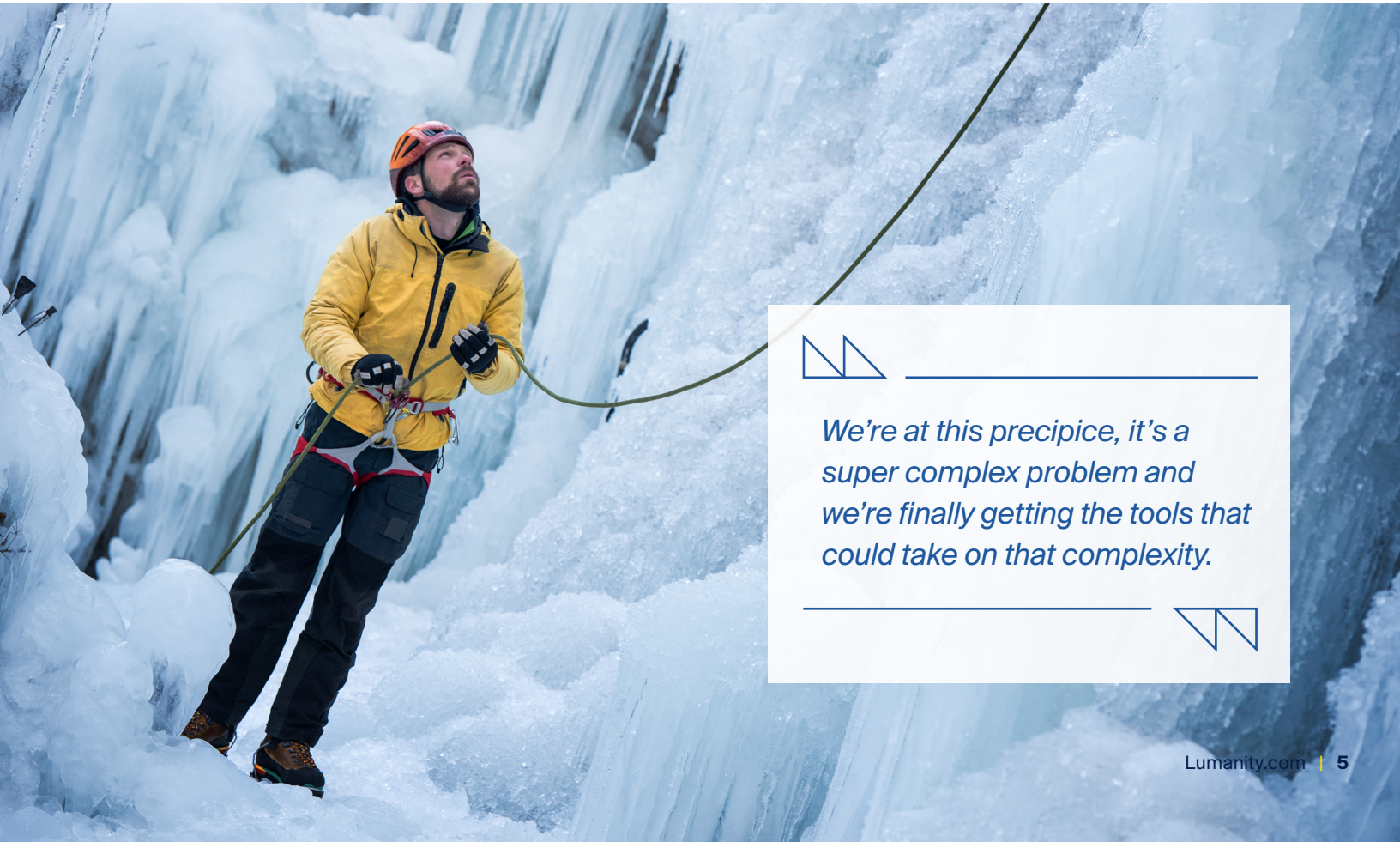
The panel agreed that one answer has to be artificial intelligence/ machine learning (AI/ML).

Guidi framed AI as a tool for handling complexity at the scale human teams cannot manage alone. **“We’re at this precipice, it’s a super complex problem and we’re finally getting the tools that could take on that complexity.”** The technology may be able to identify patterns in multimodal data spanning genomics, transcriptomics, proteomics, radiology, and pathology. Such insights may drive more efficient and rational research strategies and decision-making.

Su agreed, placing emphasis on biological explanation, not pattern recognition alone. **“As a field, we can interrogate CRs, and without the really good biopsies, it’s like a black box.”** He also gave a concrete example of where computational power could change the iteration cycle by learning from small datasets and adapting protocols based on those insights. **“On those 28 patients, can the AI tell me there’s a difference between the 6 [who responded and those who did not]? It’s not too small to accrue another 10 based on your AI biomarker. And you should get an 80% response rate. And then you have a lead to go for.”**

Hoos closed this thread with both urgency and caution. **“AI is the answer here. We need to investigate all the data that we have because we have it.”** He immediately added the constraint that matters for execution: **“you need to lead us to use them right. It’s not simple.”**

The practical implication for sponsors is governance. AI creates value when it improves decision quality and makes proof more decisive. That requires clear ownership of output, traceability to data sources and assumptions, and accountability that remains human and program owned. Otherwise, AI adds narrative density without strengthening proof.



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A Call to Action:
Be More Visionary

The panel ended where it began, with transformation as the goal. As Hoos closed directly: “Let's be more visionary than we have been in the last years.”

What this means in terms of actionable principles:

01 **Align the organization and its capital spend around “breakthrough” as the objective.** Taking incremental steps is allowed within this context, but a large share of finite capital should not be spent on repetitive, marginal experiments. Incentives should be.

02 **Engineer proof pathways around the breakthrough vision but also biological and operational realities.** Empirical, “spaghetti”-style exploration may be used to gain insight but must be bounded by narrowing and stop criteria. Build development plans around requirements for both transformative clinical impact and commercial viability.

03 **Invest in AI/ML and data and tissue collection for deeper and faster insight.** Make it a priority to explain response (or failure), not just observe it, so that the learnings can be used for future decisions and other programs. Use AI to improve pattern-finding and speed—with the appropriate governance.

04 **Drive innovation at the system level.** Demonstrate the need for and feasibility of reshaping development pathways and regulatory assessments to support breakthrough innovation. Push efficiencies and impact to tip the balance of how biopharma is assessed and attract a revival in funding.

A desirable pace of future breakthroughs is not inevitable. It will require commitment, large-scale investment, and wise use of talent and resources, as well as reforms at a system level. As an industry, we must learn from our successes and failures to date, organize and operate well, and take advantage of the latest science and computational technologies. But there is every reason to believe that breakthroughs are achievable. Teams that get this right won't just generate better science. They'll engineer transformative outcomes for cancer patients.



The Oncology & Advanced Therapies Forum

The real change happens when more people step forward; sharing, building, and questioning the systems that still leave too many behind.

Cancer Progress 2027 expanding to a two-day, in-person event in the heart of Philadelphia, April 14–15, 2027. The next wave of panels is taking shape now, with new voices, new data, and new questions we can't afford to answer slowly.

Whether you're a patient, sponsor, policymaker, clinician, or advocate:



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