

From Physician to Leader in Global Research and Development

A Conversation Between Ken Song, Lisa Bodei, and Johannes Czernin

Ken Song¹, Lisa Bodei², and Johannes Czernin³

¹RayzeBio, San Diego, California; ²Memorial Sloan Kettering Cancer Center, New York, New York and ³David Geffen School of Medicine at UCLA, Los Angeles, California

Lisa Bodei, MD, PhD, from Memorial Sloan Kettering Cancer Center (New York, NY), and Johannes Czernin, MD, from the David Geffen School of Medicine at the University of California Los Angeles, talked with Ken Song, MD, about his career as a physician, venture capitalist, industry CEO, and global research and commercialization leader. Dr. Song is president and CEO at RayzeBio (San Diego, CA), a targeted radiopharmaceutical company developing an innovative pipeline against validated solid tumor targets. He is also the cofounder and chair of the board at Ablaze Pharmaceuticals (Shanghai, China), which is focused on radiopharmaceutical development for the greater China market. Before RayzeBio, he was president and CEO of Metacrine, Inc. (La Jolla, CA), where he led the organization from research to midstage clinical development and also positioned the company for an IPO. He was a cofounder and, from 2010 to 2016, CEO of Ariosa Diagnostics (San Jose, CA; acquired by Roche), where he led the organization from early research to global commercialization of the Harmony prenatal test in more than 100 countries. He also served as executive chair of Omniome (San Diego, CA; acquired by Pacific Biosciences), a sequencing technology company, helping it mature from basic research to a product development company.

Dr. Song earned his BS from Massachusetts Institute of Technology (MIT; Cambridge, MA) and medical degree from the University of California San Francisco (UCSF). He trained in internal medicine at UCSF and specialized in gastroenterology and hepatology at the University of Washington (Seattle), along with a scientific research fellowship at the Fred Hutchinson Cancer Center there. Before being an operator and entrepreneur, he worked as a venture capitalist at Venrock, as well as a consultant at McKinsey & Co.

Dr. Bodei: Ken, you are currently the president and CEO of RayzeBio, as well as cofounder and chair of Ablaze Pharma. You have been president and CEO or chair of other life science companies, including Ariosa Diagnostics, Metacrine, and Omniome. Intriguingly, you have been a venture capitalist and physician. Before we delve into more specific questions, could you tell us more about your career progression?

Dr. Song: My career has been one of serendipity, driven by intellectual curiosity. I like to explore and learn new things within the discipline of life sciences. When people ask me about my favorite hobbies, I include work as one of my top interests—because I love what I'm doing. I started in medicine and had my mind set to pursue

translational research using proteomics. But then an opportunity to join a venture capital firm came out of left field. Although I was hesitant at first to pursue it, I was intrigued by the opportunity to interact with entrepreneurs and brilliant scientists who were at the forefront of innovation. Partnering with them and being able to provide them the capital to help their ideas blossom really excited me. While at the venture capital firm, an opportunity presented itself to lead a liquid biopsy company, and I decided to pivot again in my career and take on the challenge. After several years, the company was acquired by Roche, and then I had the opportunity to make another pivot into therapeutics and joined Metacrine as CEO, working on nonalcoholic steatohepatitis, which was emerging as an epidemic liver disease. Around the same time, I took on the executive chair role at Omniome, a company that drove innovation in next-generation sequencing and was ultimately acquired. In spring 2020, right around the start of the COVID pandemic, I was approached to launch a new company focused on radiopharmaceuticals. At first, I had no appreciation of radiopharmaceuticals, but, after several months of diligence, I realized the incredible potential of therapeutic radioisotopes to treat cancer. I was excited to launch a company that could focus on innovative discovery to propel the radiopharmaceutical field forward.

Dr. Czernin: When you left MIT, where you majored in biology, you picked UCSF for medical school? Why?

Dr. Song: It was about gaining new experiences. I had never lived on the West Coast. I grew up in the Midwest and moved to the east coast for college. When the opportunity to go to a great medical school on the West Coast presented itself, and I could get California residency after 1 y to reduce tuition cost, it was a no-brainer decision. I've clearly enjoyed the West Coast, because I haven't left since I came out here in 1996.

Dr. Bodei: What did you do after medical school?

Dr. Song: On receiving my MD, I joined McKinsey, a global management consulting firm. I had been a student all my life, with no breaks from undergrad to med school. Continuing from med school to residency and then fellowship seemed to me to be the same grind. I was attracted to McKinsey, because it presented the opportunity to work with companies and help them develop strategies. I worked for a couple of years as a management consultant but realized that consulting just wasn't for me. I went back to



Ken Song, MD

medicine for an internal medicine residency and then pursued a clinical fellowship in gastroenterology and hepatology in conjunction with a research fellowship.

Dr. Bodei: *Do you feel like there is a guiding principle to all your career decisions, or was it all serendipity?*

Dr. Song: I think the common thread through all the things that I've pursued is to be constantly learning and to be curious. By having been a physician, a researcher, an investor, a management consultant, and an operator of several companies, I believe I can leverage all those prior experiences help advance the field of radiopharmaceuticals.

Dr. Czernin: *Would you say that your time in venture capital was not sufficiently intellectually stimulating?*

Dr. Song: My time as a venture capitalist was incredibly stimulating, because I evaluated hundreds of different ideas, ranging from novel drugs to medical devices, diagnostics, life science tools, and health-care delivery services. However, as a venture capitalist, I felt one step removed from actually making things happen. My experience as a clinician probably shaped my interests to be an operator, because as a physician—especially as a resident—you're on the front lines making the decisions. You create or shape outcomes directly.

Dr. Bodei: *What is your approach to a problem, whether it is logistic, organizational, economic, or clinical?*

Dr. Song: I first try to find out what I know that can help find a solution. But there is something that I've learned over my career:

Dr. Czernin: *But many leaders are not exceptional.*

Dr. Song: Yes. That's why many companies regress to the mean, which is average. You can have an effective, intelligent, decisive leader, but sometimes you also need a tremendous amount of luck. Career success, relationship success, financial success—a lot of that is luck and timing. And that may be the biggest determinant of whether one is successful.

Dr. Bodei: *I'm Italian, and I know about conductors. You do need a leader, a conductor, but you also need an orchestra or (as we call it nowadays) a team. What are your thoughts about the team? How do you choose the team members?*

Dr. Song: I look for several things. Obviously, there's competence and experience. And then there's personality. And then the ability to get things done. It really matters that you get along with the person. If you hire people who are exceptional but you don't get along with them, it just doesn't work as well. If you don't want to spend time together to figure stuff out and get things done together, progress will suffer. I usually make a judgment within the first 20–30 s whether I'm going to like somebody. So, if I don't have that positive feeling, then that's a big negative. But assuming I get comfortable with that first interaction, then I am looking for knowledge/experience and the ability and willingness to just get things done. You want team members who not only can get stuff done but can get it done efficiently.

Dr. Bodei: *On with theranostics. It was surprising that you were attracted by this field, because it had a track record of business*

“Ultimately, the richness of life is in finding that thing that you feel you can put your whole heart into.”

it is just as important to find out what I don't know. That's where you must invest the most amount of time to find the people or to educate yourself to fill that gap. I ask myself, “How am I going to figure this out? Who could I call? Who could I talk to? What can I read so that I could build that knowledge to help?” You also have to balance between an ideal solution versus what is practical and realistic, taking into account limited time or resources. My time as a venture capitalist allowed me to see how other entrepreneurs identified practical, workable, and impactful solutions.

Dr. Czernin: *Once you find people who fill the knowledge gap in certain areas, how do you manage your team? Do you tell them exactly what to do?*

Dr. Song: As a CEO, it's my job to be a decisive leader. There are different leadership styles and, although some may lead by delegation, I don't think that is the most effective approach. If you look at some of the greatest innovations, they came from very decisive and strong leaders. Think Steve Jobs or Elon Musk or Bill Gates, etc. Those are very strong personalities who invested time to dive into the details. They made the decisions. They didn't hire a third party to do some market survey or market research. They took it on themselves to understand, to the best of their ability, the industry and the opportunities. They had the confidence in having the information that is necessary to make the decision and stick with it and then aligning the rest of the organization.

Dr. Czernin: *That requires a certain level of exceptionality. If you are not exceptional, then this model will fail.*

Dr. Song: Then you shouldn't be a leader.

failures. Of course, it has a much longer history in Europe, where it was highly successful but with very limited commercial success.

Dr. Song: Despite the historical business failures, the clinical success and potential were clearly evident. What we're doing with radiopharmaceuticals is true precision medicine. There's no other modality where you can take your drug and use it as the diagnostic agent to visualize where the drug is going in the human body to understand the tumor and normal tissue uptake and then select patients for treatment based on the imaging. This is about as precise as you can get. The second feature that attracted me was the existing clinical validation data within neuroendocrine tumors (NETs) and prostate cancer, two different solid tumor types. It is not a leap of faith to think that this would be applicable to other solid tumors beyond NETs and prostate. The third aspect that attracted me to radiopharmaceuticals was the lack of broad appreciation and thus lack of proper investment to drive innovation. Academia can only take things so far; whereas once industry gets involved, the amount of capital and pace at which things can get done take it to a different level.

Dr. Bodei: *Nuclear medicine has been involved with radioactive iodine since the 1940s. To now finally see large randomized and industry-sponsored studies is gratifying. But in view of all of the effective therapies that oncologists have for many cancers, do you think that there is theranostics hype? What is the destiny of theranostics? What are the threats?*

Dr. Song: This is the next major treatment modality for oncology. I see radiopharmaceuticals today similar to where antibody–drug conjugates (ADCs) were 15 y ago and cell-based therapies were 10

y ago, when both those modalities were in their infancy. Today, we have multiple ADC and cell therapies approved, with hundreds of companies now pursuing these modalities. We already know radiopharmaceuticals work. There is a pretty good road map to discover and develop novel radiopharmaceuticals if one invests the time and the energy. So, it's not hype, because we know it works. Drug discovery is still hard and takes time and commitment. Beyond drug development, radiopharmaceuticals have more complex supply and logistics challenges than conventional small-molecule drugs and biologics. I don't see that as a huge challenge, but it is one about which we need to be more proactive and mindful to ensure that all this is worked out. The future success of radiopharmaceuticals is not a question of if; it's a question of when for this modality.

Dr. Czernin: *There are different approaches to further developing the field. One would be to intensify the search for new targets. Brilliant people have been screening for other theranostic targets for decades, yet the number of promising targets has remained fairly limited. How would you approach target discovery and validation from an industry point of view? And how would you try to improve current approaches to, let's say, toxicity associated with some current prostate-specific membrane antigen-targeted radioligands?*

Dr. Song: My view is that we should not invest in novel target discovery at this time. Several clinically validated targets are already out there that have never been exploited for theranostics. There's a laundry list of dozens of targets you can just look up that have yet to be pursued for radiopharmaceutical therapy. I think the investment needs to be in finding novel ligands that bind to these known targets. One area for us to collectively push the field is in the regulatory framework for radiopharmaceuticals. We are currently wedded to external-beam radiation therapy-derived dose limits to normal organs, limiting therapeutic dosing to an unrealistic toxicity risk threshold. For example, kidney radiation dose tolerance is about 23 Gy, based on a 5% toxicity risk at 5 y. If we applied this same standard to other drugs, we'd have no approved drugs available for cancer patients. We need to look at risk/benefit ratios and use the same standards applied to all other cancer therapy modalities. Some patients are not going to be alive at 1 y, so to worry about chronic toxicity in some single-digit percentage is completely the wrong way to think about administering radiation to these patients. We may see dramatic efficacy by pushing the amount of delivered radiation to the tumors. We need to put the patients first and be data-driven based on clinical outcomes to ensure we are properly dosing radiopharmaceuticals.

Dr. Bodei: *Whenever we see a toxic effect, the spotlight is focused on radioactivity. Radiation always has a bad image. How do you think we can go about developing more efficacious treatments, with the skepticism toward radioactivity and with the skepticism toward individualized dosimetry?*

Dr. Song: It is going to take time to reeducate and reorient the public image. But if we're committed to it because we know that the current way of thinking is incorrect, then we can achieve change. Look at the gene therapy field and how that has evolved. For the longest time, everyone was freaked out about gene therapy. It was a taboo. Yet look at where we are now. People have fully embraced this modality, and many treatments are now in high demand from patients. With radiation, people think of exploding nuclear power plants or nuclear bombs. But if we reeducate people to appreciate radiation as an effective means to destroy cancer cells selectively, we can change perceptions. Let's emphasize the positives and not try to justify ourselves against the negative perceptions. In terms of developing more efficacious treatments, we need to develop radiopharmaceutical drugs like all other cancer drugs. We should be

driven by clinical data to identify the dose-limiting toxicity. Dosimetry is a useful tool but should not be used to guide clinical decisions.

Dr. Bodei: *We also need to address the supply chain problem. There are significant infrastructure problems for ^{177}Lu supply, and these are even more prominent for targeted α -therapy. What solutions do you see here?*

Dr. Song: Isotope supply is clearly a must-have for the industry and products, and there is still a limited supply, especially ^{225}Ac . The good news is that many people and companies are now going forward and investing in alternate routes of production. When you see that amount of activity, it's likely that it's going to get figured out. But it is going to take time, because this is not easy. Sitting here today, I think 10 y from now the actinium supply problem will have been completely solved, and in the interim, as various solutions come forth at varying scales, we will need to prioritize and allocate supply.

Dr. Bodei: *Absolutely. That begs the question: given all of the above, what are your future company plans?*

Dr. Song: We currently have our first program using ^{225}Ac in the clinic, which we think fulfills an unmet need in NETs. NETs constitute an orphan indication; thus, the required amounts of actinium are moderate. We are also evaluating our first drug candidate in small cell lung cancer. We are continuing to invest in our discovery pipeline, and we have several initial novel candidates ready for early clinical evaluation. Most of the therapies that we develop are likely to be tested initially in advanced-stage cancer patients. So again, this is a more limited number of patients as it relates to actinium supply needs. Even if you go after a large indication such as colon cancer and you're going into the last-line setting, you're looking at thousands or tens of thousands of patients, not hundreds of thousands. Eventually, moving into earlier-line treatment settings would be pursued. That's how we're approaching it, being methodical and realistic in terms of what we think our addressable patient populations will be for our initial products.

Dr. Bodei: *The need is rapidly growing for experts in the clinical delivery of theranostics. How should we form the new generation of physicians, entrepreneurs, and scientists to move theranostics forward?*

Dr. Song: When we try to do something new, there will always be that initial scarcity of capital, activity, and talent. How do you fix that? First, we need to see some companies be successful. As we see some successes, many others will follow, and we'll also have people who have experienced success who will go on to become the future leaders. It's like people say in medicine: watch one, do one, teach one. That principle also applies to industry. We see several radiopharmaceutical companies emerging now, and we intend to lead the charge. So, we need to give a little bit of time for people to be able to watch how it's done. In terms of the care delivery side, I do believe that close collaboration among specialties across oncology, radiation oncology, and nuclear medicine is needed. We need to avoid turf wars. Implementation will vary across countries and across institutions within the same country. There's not going to be a single construct that's going to work for every institution.

Dr. Czernin: *We estimated recently that we will need around 120 theranostic centers in the United States. We don't currently have well-trained experts to run these clinics. Yet patients will demand this highly specialized service. Where it comes from will be up to the people who have the qualification to deliver it.*

Dr. Bodei: *What do you think about combination treatments, how will these treatments be positioned, and what would clinical trials look like to test combination treatments?*

Dr. Song: Monotherapy is increasingly rare in oncology. For combination therapy, it is useful to show efficacy with the single agent first before you do the combination. Combining radiopharmaceuticals with immunotherapy is talked about widely and I think has a lot of merit for further investigation.

Dr. Bodei: *What advice do you have for our young colleagues and people who start their professional careers? What kind of life advice do you have for them?*

Dr. Song: I say this to our employees here at RayzeBio: you have to love your work. It's really a shame if you don't, because you're probably not being fully effective in what you can actually do to contribute to society. And think about the amount of time that you're spending doing something that you don't love to do. My advice to anyone is just find what it is that you get excited about and that you really want to do. You can achieve greatness. You don't have to be at a biotech company. You don't have to be

a clinician. If you love glassblowing, you can be an amazing glass artist. I tell my kids, if you love just being outdoors, then you can find many opportunities to either improve the environment or be a tour guide or lead hikes or be a conservator. Ultimately, the richness of life is in finding that thing that you feel you can put your whole heart into.

Dr. Czernin: *Thank you for sharing your journey from biology to medicine to industry and back to care delivery. We are grateful for your time, and our readers will appreciate your insights.*

DISCLOSURE

Johannes Czernin, editor-in-chief of *The Journal of Nuclear Medicine*, serves on the scientific advisory board of RayzeBio. No other potential conflict of interest relevant to this article was reported.