# George Chen â?? Co-Founder, Chairman & CEO, D3 Bio

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*Dr George Chen explores D3 Bioâ??s strategic approach to drug development, its ambition to launch two cancer therapies in the US within five years, and the critical role of partnerships and funding in achieving these goals. Reflecting on this journey, Dr. Chen emphasizes, â??Itâ??s a journey to realize a dream for patients in need.â?•*

**How did you approach the foundational strategic decisions for D3 Bio, and in what ways have these choices influenced the companyâ??s operational direction and growth trajectory?**

D3 Bio is a Cayman registered company formed in the summer of 2020. From the outset, we focused on several key considerations. The first was talent acquisition. We sought individuals with global experience and a deep entrepreneurial spiritâ??traits that are abundant in China. We are convinced a place like Shanghai offers a rich talent pool that supports this vision. In addition, our lean, agile, and stable team structure allows us to make faster decisions and maintain continuity, avoiding the organizational complexity and team turnover that can hinder larger companies. The second consideration was where to set up our discovery operation. Shanghai has a friendly ecosystem for discovery research, and is at the heart of a robust network of Contract Research Organizations (CROs) that provide the necessary scale, expertise, and cost-effectiveness for drug discovery and preclinical development. Many global biotech companies, regardless of their base, work closely with Chinese CROs for their research needs. By situating our discovery center here, we

gain direct access to this ecosystem, which is essential for driving our innovative pipeline. Cost efficiency was another crucial factor. As a young company with limited resources, we needed to maximize the impact of our capital. The economic advantages in China, combined with our ability to maintain productivity even during the challenges of the COVID-19 pandemic, have allowed us to advance our programs efficiently.

Our decision to establish D3 Bioâ??s discovery and preclinical operation in Shanghai was driven by a clear strategic vision that aligns with both our immediate needs and long-term goals. Despite some prevailing perceptions about Chinaâ??s biotech sector, I firmly believe that China is not only investable but also a critical player in the global biotech landscape. The countryâ??s economic significance, coupled with its competitive yet collaborative environment, makes it an ideal location for innovative enterprises like ours.

Our approach to clinical development has always been global in scope. From day one, our clinical trials have been designed to meet the highest international standards, ensuring that our pipeline assets are ready for global development. This strategy not only enhances the quality of our research but also positions us to avoid costly adjustments later in the process.

When it comes to building our pipeline, we chose to focus on organic discovery rather than following the trend of rapidly licensing compounds for quick market entry. We focus on actionable targets that involve mechanisms of tumor growth, tumor cell killing and resistance to standard of cares. Our goal is to discover and develop compounds that have the potential to become new standards of care. While we remain open to licensing opportunities, they are considered supplementary to our primary focus on in-house discovery. These strategic choices reflect our commitment to creating a company that is poised to make a significant impact on a global scale. By combining the advantages of our Shanghai base with a clear, long-term vision, and adhering to global quality standards from the outset, we are well-positioned to drive meaningful innovation in biotechnology.

**How do you strategically guide D3 Bioâ??s research and development in oncology to ensure differentiation and the successful creation of impactful therapies?**

At D3 Bio, we employ what we call the â??D3 approach,â• a strategy that blends knowledge, experience and judgement with disciplined scientific methodology. This approach is akin to the Chinese concept of â??é•? (dÃ o),â• a guiding principle that embraces both the visible and the invisible in shaping our actions and decisions. Having been deeply involved in the development and launch of numerous drugs in my previous roles, Iâ??ve honed an instinct for identifying where meaningful advancements could be made. Our strategy revolves around using clinical insights to pinpoint areas where we could offer significant improvements in patient outcomes.

The process begins by examining these insights to identify critical gaps. From there, we determine which biological targets to pursue in our discovery research. We focus on targets that are well-understood in their biology, rather than chasing completely novel ones, which often come with high levels of uncertainty. By choosing targets with a solid biological foundation, we can better predict how they will interact with disease processes, contribute to tumor progression, and how resistance mechanisms might evolve. Additionally, this understanding allows us to develop biomarker strategies that identify patients most likely to benefit from our therapies.

Our ultimate aim is to create compounds that are not just viable but have the potential to become blockbuster drugs. The journey from initial discovery to drug launch can span seven to eight years, during which time both technology and societal expectations evolve. Itâ??s a given that compounds will face attrition along the way. By setting a high standard at the outset, we ensure that even as

challenges arise, our compounds can still meet or exceed market expectations by the time of launch. The key to our approach is starting with a strong foundation. If we begin with a compound that already meets high expectations, it can withstand the natural attrition that occurs during development and still emerge as a market leader. Conversely, if the initial standard is too low, the compound risks falling below market expectations by the time itâ??s ready for launch, which can diminish its potential impact. In research and development, our goal is to consistently choose the path that leads to the most successful outcomes.

**In an era where many companies are increasingly prioritizing platform technologies, what led D3 Bio to focus instead on disease-specific treatments?**

While platform technologies have become the focus of many in the industry, they are not always the universal solutions they are often made out to be. At D3 Bio, we deliberately chose a different approachâ??one that prioritizes a deep understanding of specific diseases and their unmet clinical needs. Rather than following trends, we concentrate on identifying areas where we can make a meaningful difference.

For instance, although Antibody-Drug Conjugates (ADCs) gained significant attention after Daiichi Sankyoâ??s breakthrough, weâ??ve strategically chosen to focus on where we see the most potential for impact. Our approach is driven by a commitment to innovation in oncology, where we apply our expertise to develop targeted therapies, whether through small or large molecules, based on the unique needs of each disease.

By avoiding the rush towards the latest industry trends without a strong, underlying rationale, we ensure that our efforts remain focused and purposeful. This allows us to develop truly differentiated therapies that are poised to make a significant difference in patient care.

**What is the most advanced project in D3 Bioâ??s pipeline, and how has the development process unfolded?**

Our most advanced project is D3S-001, a compound currently in Phase 2 clinical trials. Over the past three and a half years, we have developed a portfolio of six assets, including three small molecules targeting the KRAS pathway, which form the backbone of our KRAS franchise, and three bispecific antibodies focused on immuno-oncology. All these compounds were independently developed by D3 Bio, showcasing our â??D3 approachâ?• to pioneering unique solutions in oncology.

D3S-001, a second generation and differentiated KRAS G12C inhibitor, has received orphan drug designation (ODD) in the United States for the treatment of pancreatic cancer, a particularly challenging disease where meaningful clinical advancements are crucial; and fast track designation (FTD) for the treatment of late line non-small cell lung cancer (NSCLC) and colorectal cancer (CRC). D3S-001 has a uniquely differentiated mechanism of rapid blockage of the KRAS G12C mutation protein with very high potency, which explains its robust anti-tumor activity. The discovery work of D3S-001 will be published in the September 2024 issue of *Cancer Discovery*. In ongoing clinical trials, this compound has shown promising early efficacy in pancreatic cancer as well as in NSCLC and CRC, specifically targeting tumors carrying the KRAS G12C mutation. To enhance its therapeutic potential, we discovered D3S-002, an ERK1/2 inhibitor, as a combination agent. Preclinical data indicate that D3S-001 and D3S-002 combination could provide more durable and efficacious anti-tumor activity, positioning our KRAS-targeting therapies as strong contenders in

oncology. D3S-002 is under phase 1 clinical development globally. D3L-001, a clinical-stage bispecific antibody (bsAb) dually targeting Her2 and CD47, is in global Phase 1 development. The unique design of this bsAb allows it to specifically block CD47 expressed on tumor cells while sparing the blockage of CD47 in normal cells and tissues. This enhances macrophage-mediated phagocytosis by removing innate immunityâ??s inhibitory signals in Her2-expressing tumor cells, creating a novel chemo-free therapy for Her2-positive tumors. D3L-001 was also granted FTD and ODD by the FDA for the treatment of Her2-positive metastatic breast cancer and gastric cancer, respectively.

D3S-001 has just completed its first-in-human (FIH) dose escalation study, which involved dosing 42 late-line advanced cancer patients across both China and global sites. D3S-001 has demonstrated promising and consistent efficacy results across NSCLC, CRC and pancreatic cancers carrying KRAS G12C mutations, as well as in patients from both within and outside of China. The discovery and development of D3S-001 reaffirms our â??D3 approachâ?•, where meaningful improvements in discovery stage could be translated into significant advances in patient care.

**With the need to accelerate development after receiving regulatory orphan drug and fast track designations, how does D3 Bio effectively manage this process, especially given your reliance on CROs and external resources?**

Accelerating development globally is indeed crucial, and at D3 Bio, we have structured our development operations to meet this challenge effectively. While we leverage the scale and advanced technologies of top-tier CROs, we maintain strict oversight to ensure all work aligns with our rigorous standards. In clinical trials, we collaborate closely with key investigators and regulatory agencies, with LabCorp and Fortrea managing trial operations and Guardant handling biomarker diagnostics. This strategic partnership model enhances our global efficiency, consistency, and presence.

Our interactions with regulatory agencies, including the FDA, EMA, Chinaâ??s NMPA, Japanâ??s PMDA, Koreaâ??s MFDS, and Australiaâ??s TGA, are frequent and integral to our development process. Drawing from my previous experience overseeing over 70 IND approvals and 30 NDAs, I have guided our small regulatory team to achieve 18 regulatory approvals from agencies of major markets, including three FTDs and two ODDs from the FDA.

Our success is rooted in producing exceptional regulatory submission packages and maintaining streamlined, effective communication with regulatory bodies. We leverage our in-house regulatory expertise alongside our CROsâ?? experience to navigate the complexities of fast track and orphan drug designations. By providing comprehensive and clear responses to queries, we often secure swift approvals, enabling us to accelerate our development timelines while upholding the highest standards of quality.

**Based on your experience with various regulatory agencies, how does interaction compare from FDA to other regulators, particularly in terms of openness and collaboration?**

The FDA is renowned for its scientific rigor and its proactive approach to supporting companies in drug development. When you present solid data with clear scientific and clinical rationale, the process tends to be straightforward. Other agencies, such as those in Korea and Japan, may introduce specific cultural or ethnical considerations into their processes, while Chinaâ??s NMPA follows its own policies, which generally are aligned with ICH principles. The regulatory timelines in

China, Japan, and Korea can be relatively longer. The EMAâ??s decentralized procedure can be longer too due to the need for consensus among multiple member states. The FDA is efficient but rigorous, particularly with programs like the Breakthrough Therapy designation that expedite the process for promising treatments. The cornerstone of success in any regulatory environment is to begin with high-quality scientific work and to compile a clear and well-structured data package. Itâ??s also crucial to approach regulatory interactions with realistic and measured expectations. Attempting to push the boundaries by posing overly â??ambitious or aggressiveâ?• questions in the hope of gaining an edge can often backfire, resulting in rejections, delays, and unforeseen complications. At D3 Bio, we prioritize what is most important for clinical outcomes and patient care. We ensure that we ask relevant questions and respond thoughtfully to the agencyâ??s feedback, implement agile project management to adapt various requests from multiple agencies, allowing us to meet their standards efficiently and progress without unnecessary setbacks.

**D3 Bioâ??s pipeline remains entirely proprietary, with no current partnerships. Is this a deliberate strategy, or have there been challenges in forming international collaborations?**

Our decision to maintain a proprietary pipeline is indeed strategic. Our goal is to advance our medicines globally, particularly in addressing major indications such as lung, colorectal, breast, and gastric cancers. Given our extensive experience in developing landmark oncology drugs such as gemcitabine, pemetrexed, lapatinib, osimertinib, durvalumab and olaparib, we understand the critical importance of timing in partnerships.

We believe that partnerships are essential, but the key is to engage at a moment that maximizes value for patients, the company, and our shareholders. This means ensuring that when a compound enters a partnership, it is well-positioned for success, rather than engaging too early before its potential is fully understood. Our approach is also flexible, considering licensing, co-development, or other forms of collaboration, but we are highly selective about when, how, and with whom we partner.

When we established D3 Bio, we raised sufficient capital to support our development work independently, allowing us to focus on building a robust pipeline without the immediate need for partnerships. However, as our clinical studies expand and require more substantial resources, we recognize that additional funding would be necessary, which is why an eventual IPO is part of our long-term strategy. This financial flexibility allows us to pursue partnerships at the right time, ensuring the maximum impact of our innovations.

**After securing $62 million in your latest Series A+ funding round, how have you navigated the current financing environment? Is the U.S. market closed for financing China-based biotechs as many believe?**

Securing capital in the pharmaceutical biotech sector is always a challenge due to the inherent risks and the critical balance between risk and return. This is the core business of venture capitalists, and our responsibility is to transform their investment into significant valueâ??turning potential into reality. During our first fundraising round, we relied heavily on our reputation, track record, vision and strategy, as we had not yet developed compounds to present.

In this recent round, however, our objective was not driven by an immediate need for capital. We believe in raising capital while we still have strong reserves, avoiding the pressure that can lead to compromised decision-making.

We demonstrated our thorough processes and high standards, which, despite our smaller size, are comparable to those of leading multinationals. This commitment to excellence has proven crucial in attracting international investment. The real question is whether you have the evidence and a compelling narrative to persuade investors that our company offers a superior investment opportunity, even in comparison to well-established players in places like Boston. U.S. investors are driven by returns, and if they see strong potential for profit, they will invest, regardless of geographic location. By maintaining a strong financial foundation and consistently demonstrating our value proposition, weâ??ve successfully navigated the complexities of the current financing environment. Our strategy of raising funds while in a strong position ensures that we can continue to execute our vision without compromising on our goals.

**Could you tell us about your team and how you source talent, particularly with the recent addition of Dr. Antoine Yver to your board?**

Dr. Antoine Yver is a Swiss-French oncologist with whom Iâ??ve had a longstanding professional relationship since early 2013 when I joined AstraZeneca Global Medicines Development (GMD) where he was leading oncology efforts. Our collaboration began when AZ, under CEO Pascal Soriot leadership, focused on building a robust R&D capability in China, and Antoine played a key role in this mission.

Our shared vision and values strengthened our professional bond over the years, and we remained connected. It was a natural decision to invite him to join D3 Bio, first as a consultant and then as an independent board member. Antoine brings a wealth of experience, a broad network, and complementary perspective that greatly benefits our team. Despite being based in France, we maintain close communication through Zoom and regular calls, ensuring his insights are always within reach. Antoineâ??s addition to our board is part of our strategic approach to grow D3 Bio. We seek individuals who not only possess exceptional expertise but also align with our companyâ??s vision and values.

**Building and retaining a strong team in Shanghaiâ??s competitive biotech environment is no small feat. How have you approached this challenge at D3 Bio?**

Attracting top talent in a competitive market like Shanghai is indeed challenging, especially when weâ??re vying with both other biotechs and multinational corporations for the same pool of talents. However, weâ??ve managed to build a strong team by being strategic and patient in our hiring approach. We have an outstanding HR leader, and through our network, weâ??ve connected with key individuals who have become essential to our success.

From the beginning, weâ??ve been highly selective in our hiring process, prioritizing quality over quantity. Each team member at D3 Bio is expected to be both a leader and an active contributor, driving the companyâ??s success forward. Our interview process is rigorous; we look for candidates who exhibit not only the necessary skills but also a deep passion, commitment, and the ability to handle both success and setbacks with composure. Over the past three years, weâ??ve carefully grown our team to 51 members. Instead of expanding rapidly, we focus on ensuring that every hire aligns with our values and contributes meaningfully to our goals. Our interview process is thorough, incorporating challenging scenarios that help us assess how candidates think, react under pressure, and fit within our teamâ??s culture.

This meticulous approach has resulted in an exceptionally stable teamâ??something thatâ??s quite rare in the biotech industry, particularly in China, where turnover is often high. We take great pride in having nearly zero turnover, which speaks volumes about the strength of our team and the supportive environment weâ??ve cultivated at D3 Bio.

**As you look to the future, what are the key milestones for D3 Bio, and how do you plan to achieve them? Are you focusing on an IPO, forming strategic partnerships, or advancing your drug candidates through Phase 2 trials?**

Our primary objective is to advance our drug candidates into fully developed products. Based on our current progress, we are optimistic that we could launch two medicines in the U.S. within the next five years. Achieving this will require substantial capital, and while we are well-funded, additional resources will be essential to sustain our momentum of acceleration.

To secure this funding, we are exploring two main avenues: strategic partnerships and an IPO. Larger capital infusions, whether through these partnerships or an IPO, are critical to driving our drug development forward and ensuring that our candidates can become backbones of new standard-of-care treatments for specific types of cancer. If we pursue an IPO, NASDAQ would likely be our preferred market due to its mature ecosystem and strong appreciation for scientific innovation.

Our strategic focus remains on developing therapies for key cancer types, including lung, colorectal, pancreatic, gastric and breast cancers. This vision guides our exploration of partnerships that can provide not only funding but also the expertise needed to bring our therapies to market faster and more effectively. An IPO is also under consideration to secure the necessary capital to achieve our ambitious goals.

**As we conclude, is there a final message youâ??d like to share with our audience?**

Iâ??d like to highlight that D3 Bio is an organization built on agility and efficiency, with a strong commitment to excellence in both discovery and development. This positions us as an ideal partner for multinational companies looking to expand their innovative efforts. We have developed a differentiated pipeline with therapies that hold substantial clinical significance, particularly in areas like lung, colorectal, pancreatic, and breast cancers.

We are eager to engage with partners who share our vision of advancing medical science and bringing better treatments to patients worldwide. D3 Bio is well-positioned to make a significant impact on global healthcare, and we welcome discussions that explore synergies and collaborative opportunities to achieve these shared goals.

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