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April 2024

Vol - 02 Issue - 05

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LaPorta Enterprises

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April 2024

A Visionary Financial Leader Driving Biotech Breakthroughs

Mutsuki Takano, a seasoned financial leader renowned for his strategic acumen, currently holds the esteemed positions of Board Director and Chief Financial Officer at Heartseed Inc., an innovative biotechnology firm at the forefront of medical advancements. With a rich career spanning over two decades, Takano's professional journey commenced at Mitsui & Co., Ltd. in 2004, where he cultivated his expertise in risk management and international trade, laying the foundation for his illustrious career trajectory into venture capital.

In July 2018, Takano embarked on a transformative phase in his career, joining Promethera Biosciences SA, now rebranded as Cellaion, as the Japan Branch General

Manager. His tenure at Promethera Biosciences SA was marked by remarkable achievements, particularly in fundraising, where his leadership as the Japan Branch General Manager and Group CFO facilitated the successful procurement of approximately Eur50 million. This accomplishment underscored Takano's adeptness in navigating intricate financial landscapes with finesse.

Driven by an unwavering commitment to combat the global COVID-19 pandemic, Takano transitioned to a gene analysis company in 2020, where the company is trying to provide quick PCR testing services all over the Japan. In his short-term tenure as CFO, he engaged in reorganizing company back office function including series of logistics management

A portrait of Mutsuki Takano, a middle-aged man with dark hair, wearing a dark blue suit jacket over a light blue button-down shirt. He is smiling slightly and looking towards the right of the frame. The background is a light-colored, textured wall.

Mutsuki Takano

Board Director and CFO
of Heartseed Inc.



system starting from distribution of PCR testing kit through testing result provision, thereby contributing to public health initiatives keeping economic activities alive even in a part by the person non infected, while the nationwide fear to the infection tends to claim for stopping everything and staying home.

August 2020 heralded a new chapter in Takano's illustrious career as he assumed the mantle of CFO and Director of the Board at Heartseed Inc. Here, Takano's visionary leadership and financial prowess have been instrumental in steering the company toward

prosperity. Leveraging his extensive expertise, he established the Strategic Finance and Investor Relations Department, a pivotal move that has fortified Heartseed's financial framework. On the other side in business partnership development and negotiation with Novo Nordisk, he served the Heartseed special team from the perspectives of risk management. Under Takano's stewardship and agile leadership, Heartseed has secured substantial capital investments, totaling JPY6 billion, and clinched a transformative global licensing agreement with Novo Nordisk, poised to unlock unprecedented milestones

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A Journey of Hope and Innovation

In his early years, Mutsuki Takano witnessed firsthand the impact of severe asthma on his mother's life. Despite the challenges, she managed her role at a software engineering company, often needing emergency medical attention during asthma attacks. Yet, with access to medication and a supportive healthcare system, she persevered, retiring after a successful career. This experience ignited Takano's belief in the power of medication to empower individuals facing serious illnesses, enabling them to pursue their aspirations.

As Takano reflects on his tenure overseeing operations at Mitsui's Venture Capital division in the US, he recalls encountering numerous biotechnology companies addressing unmet medical needs on a global scale. "I saw mainly US companies, sometimes EU or Israel or China, but not so much about Japan companies," Takano remarks. However, Takano's journey took a transformative turn upon joining Heartseed in 2020. "Our CEO, Dr. Fukuda, showed me a video of living, beating cardiomyocytes[1] derived from induced pluripotent stem cells[2]. It was the first time I had seen such synchronicity among cardiomyocytes, sparking immense excitement within me," Takano shares.

At Heartseed, their corporate mission of "Opening the door to the treatment of heart disease through regenerative medicine" drives their innovation. Guided by core values collectively termed as "Heartseed Value," the company fosters a culture of pioneering spirit, self-driven innovation, prioritization of life, continuous growth, and collaborative teamwork.

Navigating the Frontier of Cell Therapy

In the realm of cell therapy, there exist two distinct approaches to treatment, differing in their intended duration of cell presence within the patient's body. Takano explains, "The first, exemplified by mesenchymal stem cells, involves the infusion of cells that naturally dissipate within a short timeframe, thus requiring lower safety standards and no need for immune suppressants."

In contrast, the second approach, epitomized by Heartseed, aims to prolong the presence of cells within the patient's body significantly, necessitating stringent safety measures. Heartseed's commitment to safety is underscored by requirements such as demonstrating one year of tumorigenicity[3] in animal models following cell infusion, in addition to conducting comprehensive long-term toxicity studies.

"The intricacies of the second type of cell therapy demand advanced cell technology to



Guided by core values collectively termed as "Heartseed Value," the company fosters a culture of pioneering spirit, self-driven innovation, prioritization of life, continuous growth, and collaborative teamwork



ensure both safety and stable manufacturing processes," Takano emphasizes. Heartseed's focus lies in producing ventricular-specific cardiomyocytes exclusively, mitigating the risk of arrhythmias that may arise from contamination with arterial or pacemaker cells.

Takano elaborates, "We have achieved a remarkable purity of 99+% in our cardiomyocyte production, thanks to our innovative metabolic selection process." This process, developed to eliminate non-cardiomyocyte cells, relies on the differential metabolic requirements of cardiomyocytes versus other cell types. "By implementing this strategy," Takano explains, "we can ensure the safety and efficacy of our final product, even at scale, facilitating our entry into global markets."

Highlighting Heartseed's lineage, Takano praises CEO Dr. Fukuda's groundbreaking research. "Dr. Fukuda, an esteemed emeritus professor at Keio University, boasts a distinguished career in this field," Dr. Fukuda's pioneering work, including the successful differentiation of bone marrow mesenchymal stem cells[4] into cardiomyocytes in 1999, laid the foundation for Heartseed's inception in 2015. Leveraging over two decades of research and clinical experience, Heartseed emerged from Keio University with unparalleled expertise and a wealth of cell-treating innovations.

Revolutionizing Heart Failure Treatment

The unique characteristics of cardiomyocytes beating within the left ventricle of the human heart distinguish them from other cell types. Unlike cells in tissues such as hair and skin, cardiomyocytes lack self-proliferation capability, rendering the heart vulnerable to irreversible damage in conditions such as heart failure.



"At any instance of heart damage, such as myocardial infarction, cardiomyocytes perish, leading to a gradual decline in heart function," Takano explains. "Despite advancements in guideline medications, such as the 'Fantastic 4'—comprising β -blockers, ACEIs/ARNIs, MRAs, and SGLT2is—that can improve heart performance, there remains a therapeutic plateau after maximum dosage administration."

Takano underscores the limited options for end-stage heart failure patients, noting, "While heart transplants offer a potential solution, the number of eligible patients is restricted. Alternatively, Left Ventricle Assist Devices (LVADs) provide mechanical support, but they come with significant burdens and risks, including the need for caregiver assistance in case of device malfunction."

Highlighting the substantial unmet medical needs in severe heart failure, Takano emphasizes, "The progressive decline in living cardiomyocytes directly correlates with diminishing heart function." Heartseed envisions a solution to severe heart failure through 'remuscularization'—the replacement of dead cardiomyocytes with living counterparts. Takano shares, "Our ongoing Phase 1/2 clinical trial for heart failure with reduced ejection fraction (HFrEF) involves the use of spheroids of allogeneic iPS-derived cardiomyocytes. Initial trial results have shown promising signs of cell engraftment and heart function recovery in patients within one year of treatment."

The Synergy of Finance and Innovation

"The intersection of financial management and life-saving treatments is pivotal," asserts Takano. Success in financing activities directly impacts the advancement of clinical trials and research and development efforts. In times of budgetary

constraints, prioritizing key pipelines becomes imperative, aligning with industry norms.

Takano reflects on the multifaceted role of a CFO in a biotech company. "Beyond a deep passion for improving patient outcomes, CFOs must possess a diverse skill set akin to that of a mixed martial artist," he observes. "Navigating investor demands, fluctuating market conditions, and unforeseen emergencies requires agility, resilience, and strategic acumen. Merely possessing technical knowledge is insufficient; past experiences in adversity and a robust spirit are equally vital."

In the realm of HFrEF treatment through Remuscularization therapy, Heartseed stands at the forefront of global competition. Takano proudly states. "With partnership and empowerment by Novo Nordisk for global development, we expect Heartseed Remuscularization therapy would provide transformative solutions to heart failure patients worldwide in future."

Takano recounts his achievements in financial leadership, highlighting successful equity financing rounds totaling approximately

JPY6 billion and instrumental involvement in the global licensing deal with Novo Nordisk. "While milestones bring temporary satisfaction, the pursuit of growth and innovation remains perpetual," he remarks. "As a biotech company, our focus lies in delivering Remuscularization therapy to heart failure patients, driving towards a future of improved healthcare outcomes."

"With the recent release of one-year initial data from our LAPiS study for advanced heart failure patients, excitement abounds," Takano shares. "We eagerly anticipate the future progress of our clinical trials, poised to bring hope and healing to those in need."

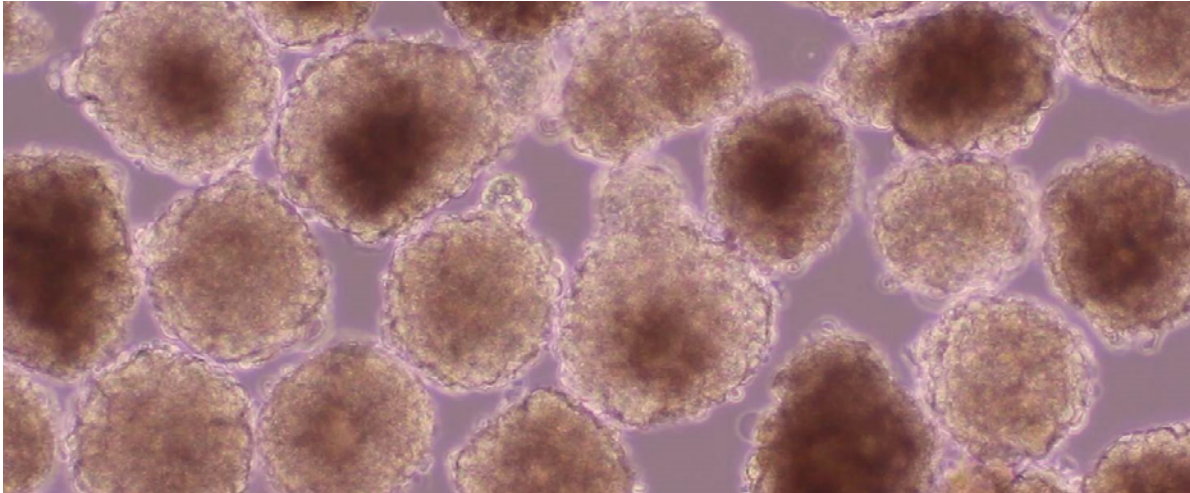
Forging Bonds

In the dynamic landscape of the biotech industry, collaboration among individuals with diverse backgrounds and perspectives is paramount. Takano asserts, "To harness collective efforts effectively, fostering mutual trust emerges as a cornerstone."

Takano reflects on the invaluable lesson imparted by a former mentor during his tenure at



Heartseed envisions a solution to severe heart failure through 'remuscularization'—the replacement of dead cardiomyocytes with living counterparts



spheroids (micro tissues) of iPS derived cardiomyocytes

Mitsui & Co.'s Private Equity Division. "Building trust entails three fundamental principles," Takano recalls. "Responsiveness, ensuring timely and accurate responses to the needs of others; Speed, delivering prompt responses aligned with expectations; and Commitment, steadfastly upholding promises made towards realization."

He emphasizes the application of these principles beyond business transactions, particularly in processes such as Due Diligence. "While Due Diligence may seem cumbersome at times, adhering to these principles transforms it into a mutual trust-building exercise,"

Takano explains. "Consistent application of these principles fosters enduring relationships and facilitates smoother interactions with stakeholders."

Drawing inspiration from his mother's journey of balancing career and family responsibilities, Takano underscores the significance of medical innovation. "As a parent myself, I recognize the profound impact of advancing medical treatments on the lives of loved ones," Takano concludes. "I am humbled to contribute, albeit in a small capacity, to the ongoing pursuit of medical innovation." ■

[1] Cells in the heart responsible for contractions, playing a crucial role in cell therapy for heart disease. Regenerating or replacing cardiomyocytes offers new possibilities for treating heart conditions like heart failure.

[2] Cells created from adult cells that have been reprogrammed to behave like embryonic stem cells. They can become any type of cell in the body, offering great potential for regenerative medicine and disease modeling.

[3] The ability of a cell population transplanted into an animal to give rise to malignant or benign tumors by proliferation, one of the concerns for stem cell therapies.

[4] A type of stem cell found in various parts of the body, like bone marrow and fat. They're known for their ability to develop into different types of tissues, including bone, cartilage, muscle, and nerve tissues. MSCs were widely studied for their potential in cardiac regenerative medicine, but there are no products approved for heart diseases by FDA.