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The Vicious Cycle:

A Case of Bioventures in Japan (1990-2010)

(Summary)

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This thesis presents the development of biotechnology industry in Japan focusing on new biotechnology firms known as “bioventures.” Bioventures started appearing rapidly in the scene of biotechnology industry in Japan in the late 1990s to early 2000s. Their rapid emergence was largely influenced by positive changes in the Japan’s innovation system which includes the following. 1) Increase in the government R&D budgets for basic research. 2) Changes in legal and policy framework to encourage university-industry linkages. 3) Reforms in intellectual property. 4) Promotion of start-ups such as creation of stock markets for high growth companies and changes in commercial code law.

Within the span of a decade or so, Japanese bioventures grew rapidly from 102 in 1994 to more than 500 in 2005. According to JBA (2009), by end of 2008, the number of bioventures in Japan stood at 569 companies. By the sheer number of bioventures, this is indeed an accomplishment. Some academic scholars and the media highlighted this rapid growth to portray a “rosy picture” to the development of biotechnology industry in Japan. However, a closer analysis reveals that despite more than a decade, majority of these bioventures are very small, operating at the seed or start-up stage. In terms of pipelines, none of the bioventures’ internally developed pipelines have reached commercialization stage (either by themselves or by their licensing partners). At the end of 2009, only 20 bioventures were listed. Average sales per listed bioventure was ¥1,252 million or approximately US$14 million; and average market capitalization per listed bioventure based on June 30, 2010 market price was ¥6,947 million or approximately US$79 million.

Most worrying, all of the listed bioventures' shares and market capitalizations showed the same declining trend after IPO.

This thesis aims to scrutinize what the real issue hindering the development of bioventures in Japan is. One might argue that 10-15 years is not enough time to measure the performance of bioventures taking into account that drug research and development takes between 10 and 15 years. However, by looking more deeply into this matter, this thesis unveils that the real issue is "structural" in nature and that time would not solve the problem.

This thesis consists of seven chapters. The first chapter, *Introduction*, introduces biotechnology as a science-based industry and the importance of new biotechnology firms in the development of science-based industry. Two distinctive characteristics of science-based industries are the importance of science as the main source of innovation and the intensity of R&D and patent activities. The *Introduction* chapter also details the thesis's research design which includes research methodology, sources of data, and research scope. This thesis uses case study approach in our attempt to understand why bioventures in Japan have not been successful. We focus on listed bioventures by providing an overview of all the 20 listed bioventures in Japan followed by a detailed analysis of two of the listed bioventures.

The second chapter, *Literature Review*, gives a broad overview of national innovation system before focusing on the previous arguments regarding biotechnology industry in Japan. This is followed by a discussion on two main sources of funding for

new biotechnology firms which are venture capital and public equity. In the last section of *Literature Review*, this thesis offers how the research question fits in the line of previous arguments and how this study contributes to the existing research. In this chapter, we maintain that the issue of funding is overlooked by many scholars and previous research in the area biotechnology development was heavily focused on university-industry linkages.

The third chapter, *Overview of Biotechnology*, defines biotechnology and reviews the history of modern biotechnology industry in the U.S. We discuss the process of drug discovery and development which exhibits high R&D cost, long development period and high level of uncertainty. Prior research has estimated that it takes an average of 10 to 15 years and US$802 million for a drug to be approved. This indicates that biotechnology in pharmaceutical needs substantial amount of funding and development time. We also compare the key indicators of biotechnology industry among selected developed countries such as the U.S., U.K., Germany and Japan. We find that Japan's biotechnology industry is smaller than most of the above mentioned countries in terms of revenue, overall employment, total venture capital investment and total number of biotechnology drugs under development.

The fourth chapter, *New Biotechnology Firms in Japan*, examines factors leading to the rapid emergence of bioventures in Japan and analyzes their present conditions and status. We find that despite positive institutional changes such as increase in university-industry linkages, relaxation of investment and financial laws and reforms in intellectual

property, majority of the bioventures are still “small” and “undeveloped”. We argue that missing in the picture is the lack of a supportive funding system for bioventures. Particularly, the current venture capital and IPO funding system create structural impediments to the development of bioventures. In terms of venture capital funding, Japan’s yearly venture capital investment is about 10 times less than the venture capital investment in the U.S. In addition, contribution from pension funds in Japan remained tiny, amounting to less than 3% of the total venture capital funding in Japan from 2001 to 2008. The 1997 investment rules that were made to allow pension funds to invest in venture capital did not have a large impact on venture capital funding in Japan. In terms of IPO funding, the money raised by bioventures had reduced drastically since 2005. The lack of participation by institutional investors in Japan’s emerging markets makes it difficult for bioventures to procure large sum of continuous funding from public equity.

The fifth chapter, *Overview of All the Listed Bioventures,* presents the analysis of 20 listed bioventures in Japan in terms of their profile, entrepreneurs, management team, university-linkages and funding. Using them our yardstick, we argue that some of the past research about Japanese bioventures such as low entrepreneurship, lack of university-industry linkages, etc. no longer hold true. We show that bioventures display signs of higher entrepreneurship; greater mobility among top management positions; experience management team and stronger university-industry linkages especially after 2000. In spite of that, when it comes to funding, many bioventures continue to struggle with the lack of funding particularly venture capital funding during their early years of

establishment and small amount of funding from IPO market. This chapter also points out that all of the listed bioventures experienced a declining stock performance after IPO. The slumping stock trend could indicate the beginning of a vicious cycle in bioventures.

The sixth chapter, C*ase Studies: AnGes MG and NanoCarrier*, focuses on the case study for this thesis. Based on detailed contextual analysis, we capture the two bioventures' experiences and journeys, starting from their establishment until the present time. Our analysis includes their history of establishment, entrepreneurs and founders, technology and patents, pipelines and drug development process; financials and sources of funding. In this chapter, we stress that funding is the real issue hindering the development of bioventures and suggest that the lack of funding caused a vicious cycle to develop in bioventures. The lack of funding slows down the R&D process which in turn results in fewer pipelines and fewer alliance opportunities with pharmaceutical companies. Faced with funding limitation, these bioventures face challenges in the hiring of skilled researchers and scientists. Their tight R&D budgets restrict them to work only on selected pipelines out of many candidates. Given the uncertainty in drug R&D, the selected pipelines are subject to failure risk. When the pipelines fail to produce any positive results, drug development process is further delayed and this could cause them to miss previously targeted milestones. This inevitably leads to a decrease in investors' confidence and declines in the overall stock prices and valuation. The slumping stock prices make it difficult for any bioventures to obtain further funding, aggravating the funding issue and the vicious cycle become more entrenched.

The last chapter, *Conclusion and Implications*, summarizes the main arguments for this thesis regarding bioventures in Japan and presents implications to this research. In terms of policy implications, we suggest an increase in the amount of venture capital investment from the pension fund system and the establishment of government funds for commercialization. In terms of managerial implications, we suggest bioventures to take a more proactive role in exploring global opportunities including funding and market opportunities.