ON GROWTH OPTION FOR R&D CONTINUITY OF BIOTECH START-UP UNDER UNCERTAINTY

Takao Fujiwara[1]

Abstract: *For biotech drug-discovery start-ups, even although the constraint of managerial resources is very severe, it takes more than 10 years for them to transfer a project from laboratory study to some products on the market. In order to increase robustness against financial crisis for continuing R&D, we examine the flexibility value of real options, and especially pay attention to the function of growth options for business entry and exit.Through a case study of a Japan's pioneering start-up in the regenerative medicine, J-TEC, we consider a survival strategy during the valley of deficit from a perspective growth option. Finally, we apply stochastic optimization to select the pipeline candidates from alternative projects.*

Keywords: Biotech start-ups, real options, growth option, and stochastic optimization

---

[1] Toyohashi University of Technology,1-1 Hibarigaoka, Tenpaku,Toyohashi, Aichi, 441-8580, Japan
fujiwara@ace.tut.ac.jp

Introduction

At the research background, since the financial crisis in 2008, the possibility of difficulty of Research and Development(R&D) continuity is very high for biotech start-ups due to the long time to build or the valley of deficit. At the time, a research question is: how can it continue R&D projects of biotech start-ups at the trade-off between the investment reluctance of Venture Capital (VC) and capital market and the continual progress of life science as antibody preparation, regenerative medicine, and personalized medicine?

As definitions of key concepts, firstly, start-ups are defined as the portfolio of real options, by considering entrepreneurs' ideas as investment opportunities (Smith, 2004). Next, real options are the investment decision tools that use such anasymmetric return idea of financial options as both downside risk hedging and upside opportunity exploiting, at the irreversible investment in real assets as R&D projects under uncertain returns (Dixit & Pindyck, 1994). One of potential of real options is dependent on the value of strategic flexibility.

So far I have already proved the effectiveness of real options for overcoming the valley of deficit to biotech start-ups within some extent (Fujiwara, 2008a). I have also showed the function of Options-Games with integrating real options and game theory for optimizing the trade-off between the flexibility value of real options from waiting the reduction of uncertainty and the commitment value for preventing rivals from entering into the market (Fujiwara, 2008b). And I have studied the timing options based on infinite American call option of assets with dividend, for explaining about the numerical difference of biotech start-ups between Japan and the USA (Fujiwara, 2010).

As the framework and methodology to above research question and from research steps, we will examine Dixit model about switching options on business entry and exit, for evaluating the value of inertia decision making to try keeping the status quo in the same real options category (Dixit, 1989). His model especially grasps the decision retaining characteristic related with sunk cost under uncertainty by Hysteresis. After that, I will try to modify this existing model by adding the growth option for explaining the aggressive motivation of innovative entrepreneurship.

The research objective is to make clear the relationship between the survival of biotech start-ups and the decision retaining function of real options.

This paper's organization is consisted of,firstly the analysis of present investment condition for R&D continuity of biotech start-ups, secondarily the fundamental theory of decision retaining function in real options, thirdly the consideration about the robust strategy against the valley of deficit based on a case study of public start-up in the regenerative medicine in my local area, and finally the trial of application of stochastic optimization to select project candidatesfor product pipeline.

2.ANALYSIS OF PRESENT STATE AND REAL OPTIONS

2-1.Biotech Start-ups' IPO Condition in Japan and the USA

Comparing with the USA, the condition of Japan's ecosystem to support biotech start-ups has been not enough in commercializing the research findings from life science. But, in addition to existing Japan Bio-industry Association, Japan Biotechnology Council was recentlyfounded by total 20 companies including main biotech start-ups and venture capital firms on July 1st, 2009. The objective of establishment is to propose the policy to the government for enrichment of social infrastructure supporting the survival and growth of biotech start-ups. There are 26 public biotech start-ups as of September 1st, 2011, including 4 companies in 2008, 4 companiesin 2009, 1 company in 2010, and 1 company in 2011, in the last case, RaQualia made an initial public offering on the JASDAQ Growth on July 20th, 2011. Further, SymBio Pharmaceuticals and 3D Matrix are planning each IPO on the JASDAQ Growth on October 20th and October 24th, 2011 respectively.

From the severe IPO market condition, there were some cases that VC firms enforced some biotech start-ups buy back their unlisted stocks from the reason of near the fund maturity, even though start-ups' R&D budgets were not enough. On the other hand, Takara Bio and R-Tech Ueno have been both black in ordinary profits from contract manufacturing for another companies. Further, OncoTherapy Science has been black in ordinary profits since FY 2008 (period end: March), from milestone revenues including out-license contracts of anti-cancer peptide vaccines with Otsuka Pharmaceutical in January 2008 and with Shionogi in February 2009 respectively, and out-license contracts of central nervous system therapeutic drug with Otsuka in March 2010. OncoTherapy Science's another partners include Fuso Pharmaceutical Industries and Ono Pharmaceutical. An anti-cancer peptide vaccine, OTS102 is a candidate of anti-cancer therapeutic vaccine with the expected efficacy ofAngiogenesis Factor Inhibitor, an interrupter against feeding to cancer cells,targeting to a tumor-cell specific partial protein, Vascular Endothelial Growth Factor Receptor 2 (VEGFR2). OncoTherapy Science is doing its clinical trial in phase II/III, and has another anti-cancer vaccine OCV101 in clinical trial phase II. OncoTherapy Science is going clinical trial in phase I/II for another vaccine, TSGC-A24 in Singapore, and is also preparing another clinical trial in France.

Thus, the number of Japan's biotech start-ups is about 500 companies, in which about 1/20 are public companies. But the USA has about 1,500 biotech start-ups, in which about 1/5, that is, about 300 are public companies. Then Japan's biotech start-ups' activity condition is less than the USA in terms of total company number and also the public company to total company ratio. Even so and severe capital market condition, hence there are some biotech start-ups which succeeded in significant fund raisings for R&D through strategic partnership as license agreements.

In the USA as an advanced biotech country, during the period including financial crisis, Y2007, Y2008, and Y2009, operating financial metrics are Sales/Revenue:$89.6B (Billion), $99.5B, and $91.6B, R&D Cost: $23.0B, $23.7B, and $19.3B, and Net Income:-$0.6B, $3.7B, and $4.3B (Table 1). Although revenue and R&D cost are reflecting the economic environment, biotech industry's net income has become historically for the first timepositive based on public companies' financial data. This possibly shows the exit period of biotech industry. During the same period, capital metrics are IPOs: $2.0B, $6.0M (Million), and $1.1B, VC: $4.4B, $4.5B, and $4.2B, Partnering Capital: $23.0B, $20.0B, and $36.9B, Market Capitalization: $454B, $404B, and $346B, and Cash & Equivalents: $71.2B, $75.6B, and $74.7B(Burrill& Company, 2009; Burrill& Company, 2010). Thus during this period, fund raisings aregoing down from VC and are rebounding from IPOs and partnerships. VC is reluctant to invest risk money from passive capital market condition. But strategic partnership is strongly rebounded since big pharmaceutical companies wish to in-license or acquire small biotech start-ups. Although market capitalization is declined, cash and equivalents are almost constantly kept, because growth options as valuation of technological potential by market investors is still high.

Table 1 Biotech Industry's Financial Evolution in Financial Crisis ($ Billion)

Year / Indices	2007	2008	2009
Sales/Revenue	89.6	99.5	91.6
R&D Cost	23.0	23.7	19.3
Net Income	-0.6	3.7	4.3
IPOs	2.0	0.006	1.1
VC	4.4	4.5	4.2
Partnering Capital	23.0	20.0	36.9
Market Capitalization	454	404	346
Cash & Equivalents	71.2	75.6	74.7

(Data: [Burrill& Company, 2009; 2010])

Additionally such companies' stock prices as Human Genome Sciences, Dendreon, and Targacept have suddenly jumped up by reflecting excellent progress of product pipelines (Burrill& Company, 2010). Thus innovative capabilities of technology development have the possibilities showing robustness against financial crisis. Further, it is forecasted that big pharmaceuticals companies, big biotech companies, and biotech start-ups are hereafter facilitating strategic partnerships among them. Big pharmaceuticals companies have been receiving the pressures to change themselves into biotech companies from chemical companies due to regulation enforcement, the patent cliff of blockbuster drugs, drug price reduction, and entrance of generic drugs. Big biotech companies consider this time's financial crisis as chance, because they have some robustness from financial healthy condition. And biotech start-ups have not enough financial robustness, in spite of their innovative technological potential. Specifically there are some emerging large M&A examples at earlier stages as clinical trial phase I or even preclinical stage rather than previous common clinical phase II trial.

2-2.Modified Hysteresis Model of Real Options

2-2-1.Exisiting hysteresis model for decision retaining function

The relationships between uncertainty and decision retaining on business entry or exit are studied to modify Marshal's threshold criteria with sunk cost under uncertainty and are modeled with analogy of hysteresis by Dixit (Dixit, 1989).

If assume μ=project growth rate, ρ = CAPM (Capital Asset Pricing Model), the relationship between both is $\rho > \mu$, σ = volatility, c = operating variable cost, I_E = entry sunk cost, and I_X = exit sunk cost, investment criterion, C_I, and abandonment criterion, C_A, of Marshal's trigger prices are respectively,

$$C_I = c + \rho \cdot I_E$$
$$C_A = c - \rho \cdot I_X$$

These mean following optimal guideline that if asset market price $P > C_I$, then optimal behavior is entry (entry price = P_H), and if asset market price $P < C_A$, then optimal behavior is abandonment (exit price = P_L). During both criteria like hysteresis curve, if the price is in the interval path $P_H \rightarrow P_L$, the guideline shows the optimal decision is project continuing even in deficit, and if the price is in the interval path $P_L \rightarrow P_H$, then the guideline indicates the optimal decision is the wait to invest until enough large profits (see Figure 1). Basically, the size of the interval mainly depends on the interest rate and sunk cost in the mean reverse and steady state condition. That is, if the environmental condition is certain, the sensitivity to irreversibility of investment is low.

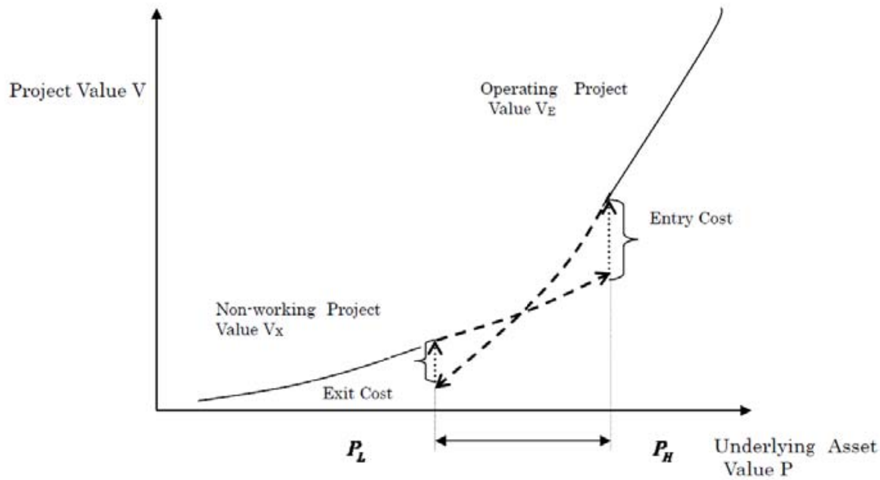


Figure 1 Concept of Existing Hysteresis Model

At Dexit model of business entry and exit under the uncertain condition which can be modeled as random walk by geometric Brownian motion of the price behavior, if like the close deterministic condition, then the condition approaches to Marshal's criteria by P_H C_I and P_L $C_{A.}$ However, if risk appears , in addition to each positive sunk cost I_E>0and I_X>0, then the distance between P_H C_I and P_L C_A enlarges and the interval of present condition retaining path becomes longer. That is, because the waiting option has positive value for identifying the future condition in spite of immediate decision under risk environment, the trigger price of entry $P_H > C_I$ and the trigger price of exit $P_L < C_{A.}$ Then the range of criteria becomes expanded as operating companies endure in deficit and closed companies become reluctant to enter.

Further with the increase of project growth rate like the high tech industry, both P_H C_I and P_L C_A decline. Then this parameter condition may explain about the USA biotech industry that in about 1500 biotech start-ups, almost all companies are in deficit except a few dozen companies since easy entrance condition and lower exit threshold.But if assume dividend as since CAPM = + then high means lower later exercise of timing option. That is, there is a trade-off between lower entry threshold and earlier decision to enter.

2-2-2. Growth option hysteresis model

Existing hysteresis model can more clearly explain about the exit reluctant behaviors of biotech start-ups by decision retaining function with sunk cost. They are facing the valley of deficit because they have only platform technologies or drug candidates without products on the market. However this model recommendsthe waiting of entry until the entry gets the project value equal or more than the summation of sunk cost as entry investment and the waiting option. Hence it is difficult to explain the entry behaviors of so many biotech drug-discovery start-ups even in deficit. At a timing option assuming the infinite American call option as business opportunity, the dividend as the opportunity cost fromthe waiting option facilitates the business entry. But as hysteresis model mainly depends on the sunk cost and the waiting option, it is contradictory to daring immediate entry into long-term deficit condition without waiting until the stage with enough large profits.

Therefore, to modify the existing hysteresis model for explaining more clearly the massive entering behaviors of biotech start-ups, we will focus on the growth option, because it is considered to share the higher ratio of high tech company value.

When measuring conservatively the project value, assume a neutral asset price $P_N$the cross point between following both curves, the operating project value V_E and the non-working project value V_X. If assume $\sigma = \mu =$ constant and early entering price = P_E,then $P_L < P_E < P_N < P_H$. That is, as P_E reflects the valley of deficit, $P_E < P_N$.

When let $V_E(P_E)$ = the value of operating project at P_E, and $V_X(P_E)$ = the value of non-working project at P_E, it also reflects the valley of deficit,

$$V_E(P_E) < V_X(P_E)$$

If further invest the sunk cost, I_E = entry cost,

$$V_E(P_E) < I_E + V_X(P_E)$$

However when let $O_G(P_E)$ = growth option value at P_E, the possible condition of entry is, as Figure 2,

$$V_E(P_E) + O_G(P_E) \geq I_E + V_X(P_E) \quad [2-1]$$

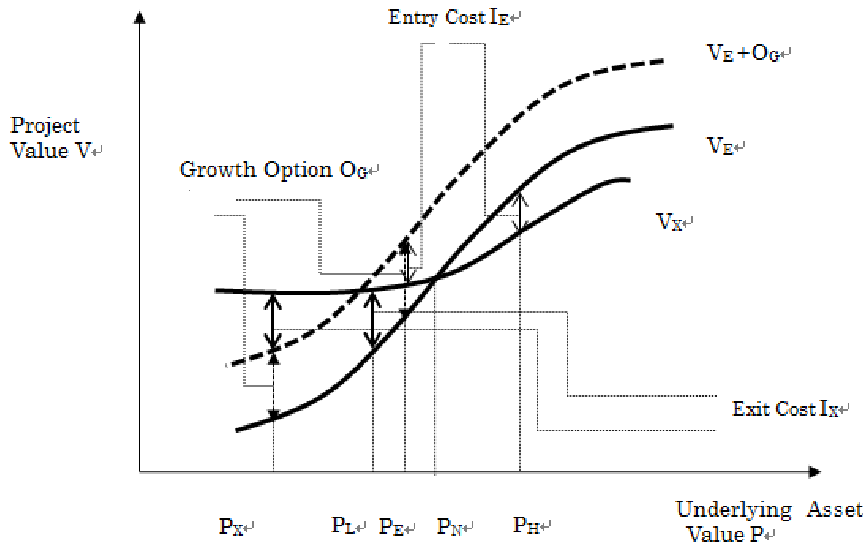


Figure 2 Growth Option Hysteresis Model

On the other hand, the condition of growth option for possible entry is,

$$O_G(P_E) - I_E = V_X(P_E) - V_E(P_E) > 0 \; [2-2]$$

For the allowance of entry by switching option between entry and exit, if $O_{D:X\ E}(P_E)$ = the value of waiting option,

$$V_E(P_E) \geq V_X(P_E) - O_G(P_E) + I_E = O_{D:X \rightarrow E}(P_E) + I_E \; [2-3]$$

Thus, even if the present sate is in deficit, when the summation of the growth option as the growth potential of biotech start-ups and the value of operating project is equal to the summation of the sunk cost as entry investment and the value of non-working project, the rationale of investment is supported. Or if the increment of the growth option to the sunk cost is equal or more than deficit size in entry, the entry decision can be reasonable. Further let the difference of the non-working project value from the growth option value as the waiting option, and if you can get the project value equal or more than the sum between the waiting option and the entry investment as sunk cost, the entry decision is possible even into long-term R&D projects.

And for more general model by modifying existing hysteresis model through introducing growth option, the trigger prices of not only entry but also exit are necessary. If assume underlying assets price P = exit trigger price P_X,

$$V_E(P_X) << V_X(P_X)$$

From Figure 2, when exit occurs from operating project to non-working project with switching option, and consider the value of waiting option, the necessary criterion is,

$$V_X(P_X) \geq I_X + O_G(P_X) + V_E(P_X) = I_X + O_{D:E \to XE}(P_X) \ [2-4]$$

And as this time shows much deeper valley of deficit,

$$I_X + O_G(P_X) = V_X(P_X) - V_E(P_X) > 0 \ [2-5]$$

Hence the function of growth option in waiting option is to facilitate the entry and to relatively prevent the exit at the switching option from operating into non-working project. Similarly the depth of valley of deficit can show the difference of growth option from entry investment at entry trigger price and otherwise the sum of growth option and exit investment at exit trigger price.

Therefore, at the biotech start-ups whose share of growth option is higher in company value, each trigger price of entry and exit is tend to become lower than these of companies in stable business. As the result, many companies enter even in deficit. And the exit depends on the success of milestone of drug development.

Such decisions of business entry and exit, continuity of R&D as learning option, and decision retaining on entry and exit can be applied to decisions on drug discovery at biotech start-ups (Copeland, 2001). But in the future, the relationships among growth option, business growth rate, and dividend must be more cleared.

3. A CASE STUDY OF J-TEC

Here we study a short case for identifying the importance of real options thinking. The case company is Japan Tissue Engineering Co., Ltd. (J-TEC), a biotech start-up for regenerative medicine located in Gamagori city, Aichi, Japan, which was spun-off from an ophthalmologic instrument maker, Nidek Co., Ltd., based both on the basic research ideas on tissue engineering in Nagoya University and on a regional public incubation supporting system by Aichi Science and Technology Foundation, as a PPP (Private-Public Partnership)

3-1. Founding History

In 1994, Nidek which had been founded in 1971 organized “21 Century Committee” for searching into new business frontiers and preventing the opportunity loss come from maturing of existing business, and appointed 2 committee members during 4 years predetermined period without budget constrains for search activities. Former president’s guidelines for new business area included the market size ¥100billion, annual sales¥10billion and annual profits ¥1billion. And rejected business areas were defined as automobile and amusement, because the automobile is a major industry in the local area and the amusementis not the manufacturing industry.

After the search, the extracted business candidates were the agricultural plant factory suitable for rural regional agriculture industry, the internet utilizing medical information service related with IT(information technology) industry, the solar battery, functional water, and health foods in resources and energy, and the home health equipment, medical laser, and tissue engineering in healthcare. Finally, the tissue engineering was selected from a perspective of market growth and synergy with existing ophthalmic equipment business.

As the institutional background of foundation, when joining the “organ engineering seminar” held by Aichi prefecture’s Science and Technology Foundation which was and is seeking post-automobile industries for next generation, they aligned strategic partnerships with Nagoya University, INAX(present LIXIL), Toyama Chemical Co. Ltd.(present a member of Fujifilm group). And from this institutional supporting system, they could get venture capital investment from Central Capital (present UFJ Capital). After 1 year preparing period, with 7 transferring employees from 3 member companies, by appointing President Mr. Yosuke Ozawa, a son of former Nidek president, and a senior managing director Mr. Toshihiro Osuka, a member of “21 Century Committee,”J-TEC was founded on February 1st, 1999, based on capital ¥100million.

3-2.Fincial Indices

J-TEC selected regenerative medicine or tissue engineering (medical device) rather than drug discovery, expecting shorter period of the valley of deficit. They have been involving with domestic pioneering projects to establish national governmental protocols or standards, while getting medical regulation approval for regenerative medicine.

For tissue culture of human autologous epidermal, they use mouse feeders and bovine cell culture medium. At the time, it is necessary to prove technologically not only enough sorts of cytokine secretion from grafted skin cells as normal skin cells, but also non-effects to patients from animal cells. Hence they tried data collection in cell banks. As a result, before medical products, they received the approval of selling the human cultured cells for researchsupport to the medicine for external use or cosmetics in May 2005. Next, they received the production approval relatively earlier among domestic biotech start-ups, for autologous cultured epidermal in October 2007, after acceptance of application for confirmation in March 2002 (see Figure 3). Therefore in the future, the increase of their revenue is expected with increasing sales of existing products and enhancement of product pipeline. However at present, operating loss may account for a large weight from the regulation standards for reimbursement, limit of certified medical facility, and necessary proactive R&D investment. But the operating loss seems smoothly showing the suppression trend after each opportunity of business revenue growth

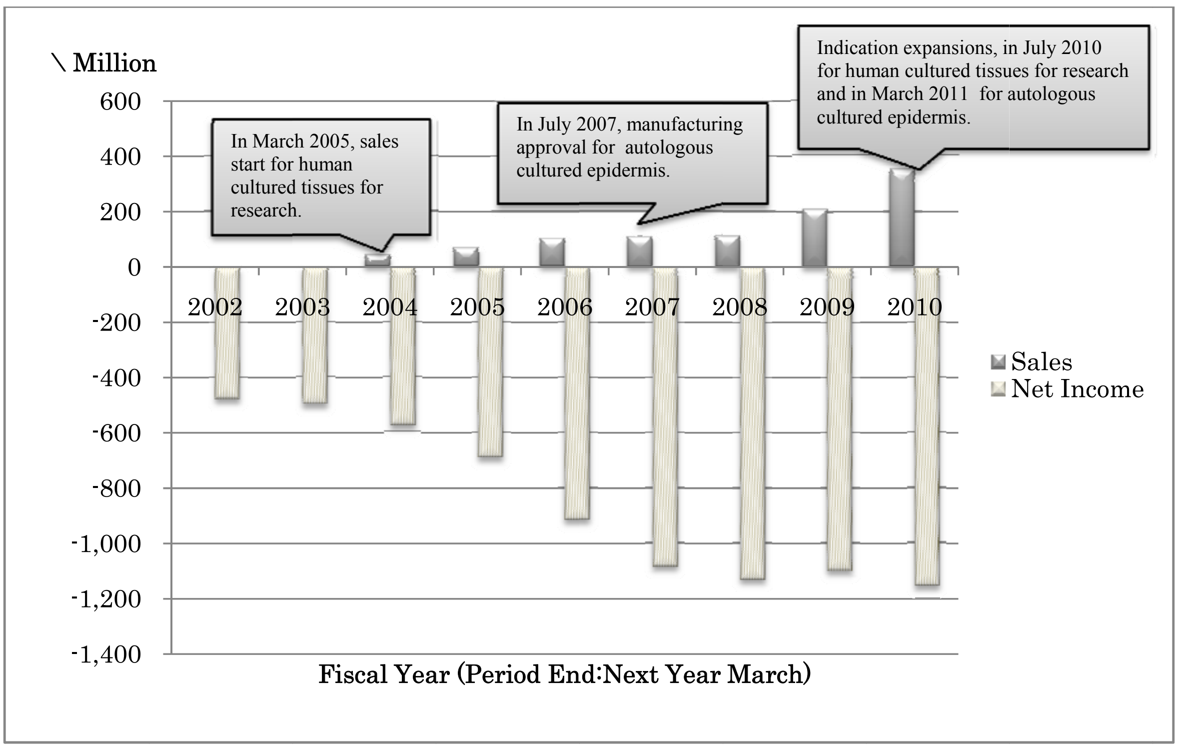


Figure 3 J-TEC's Business Revue Indices (Data: J-TEC home page IR, 2011)

While operating cash flows have the possibility of future improvement, they have invested respectively on new office building in 2004 and on R&D in 2005, even in deficit condition (Figure 4). However the cash equivalent assets as money in hand show the financial health to continue R&D, with their-party allotment to VC firms in 2006, IPO on the former NEO (present JASDAQ Growth) in December 21st, 2007, with the production approval in October of the same year.

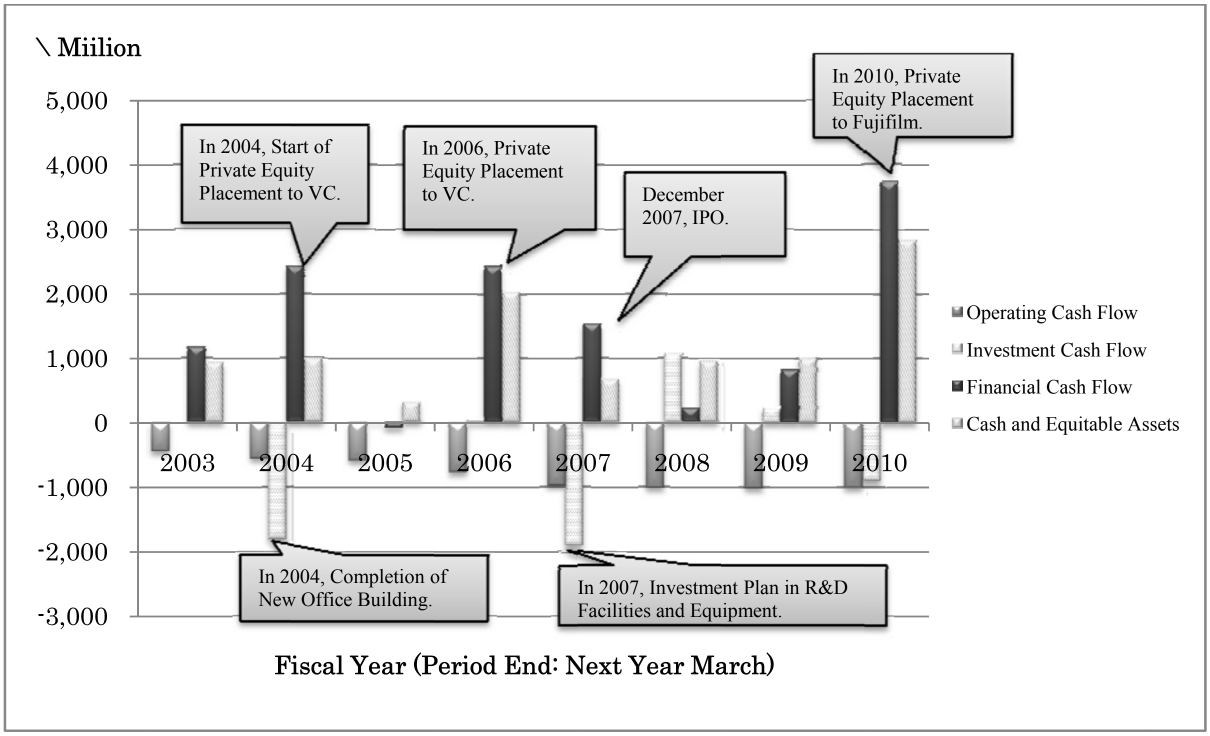
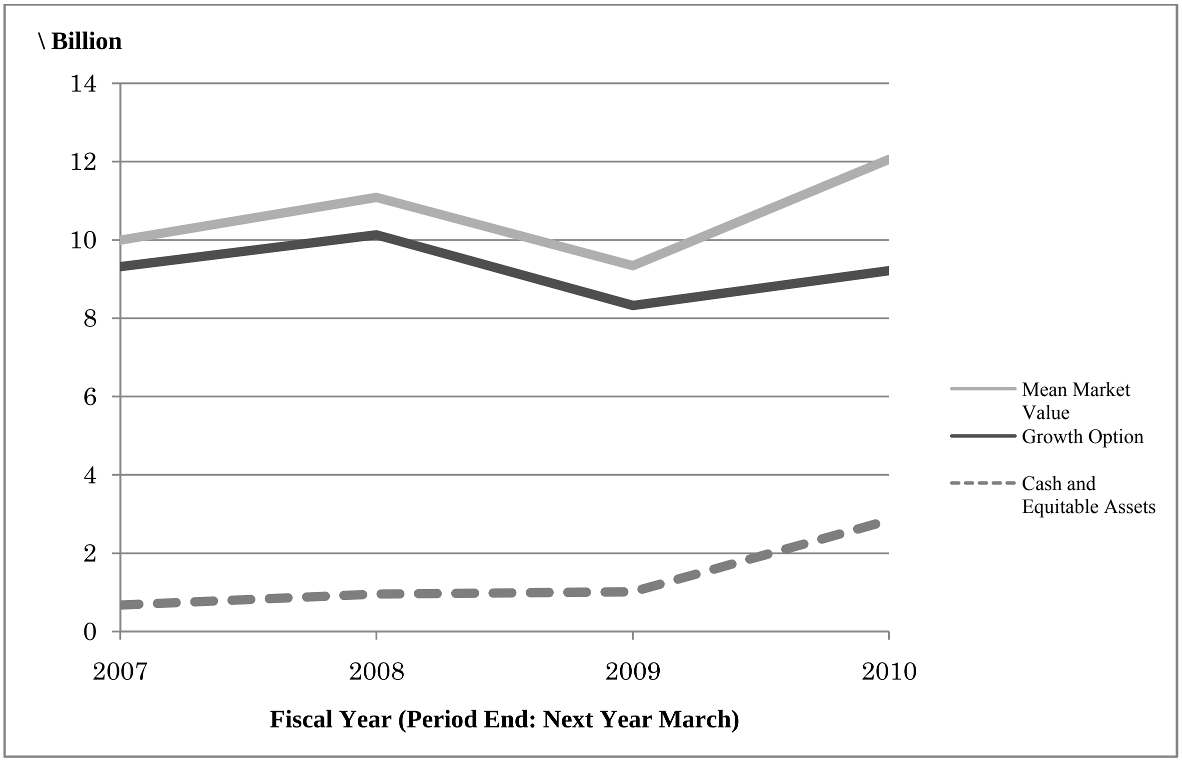


Figure 4 J-TEC's Cash Flow Behavior (Data: J-TEC home page IR, 2011)

As a supporting evidence for their financial robustness to the valley of deficit, the weight of growth option (calculated as the average market value based on stock issued minus the cash equivalent assets) in the market value of company have been constantly high in spite of a fluctuation (Figure 5). Hence if the promise of technological potential is evaluated from capital market, it may be possible to raising funds for R&D from such market.



(Data: Nikkei.com and J-TEC's home page IR, 2011)

Figure 5 Evolution of J-TEC's Technological Potential

Additionally Fujifilm increased the capital in entering into life science business by way of Toyama Chemical in October 2010 (Table 2). This is an acceptance capital equitable to the strategic partnership based on license with big pharmaceutical companies. And they established the office in Singapore in December 2010 by the strategy emphasizing emerging"Asia."

Table 2 Change of J-TEC's Recent Main Stockholder Rank with Capital Tie-up

Rank	FY 2009 (Period End: March 2010)		FY 2010 (Period End: March 2011)	
	Stockholders	Ratio of Shareholding (%)	Stockholders	Ratio of Shareholding (%)
1	Nidek	19.07	Fujifilm	41.29
2	Toyama Chemical	7.73	Nidek	11.56
3	INAX	4.19	Toyama Chemical	4.53
4	Mitsubishi UFJ Capital	4.05	LIXIL(former INAX)	2.45
5	JAFCO Biotechnology I Investment LP	1.88	Mitsubishi UFJ Capital	2.37

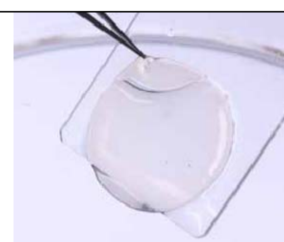
(Data: J-TEC home page IR, 2011)

3-3.Product Development Process and Pipeline

The basic function of biotech start-ups is an applied research to commercialize the basic research findings from universities into the product on the market even if niche markets. The product portfolio includes, within now only publicly opened items by them, autologous cultured chondrocytes and autologous cultured corneal epithelium (related with Nidek), in addition to autologous cultured epidermis on the market and the service of cultured human tissues for research support (see Table3). In the global skin market, there are other segments like epithelium outside epidermis, and not only the USA but also South Korea succeed in the products on the market. Hence in spite of regulation industry, if focusing on global market, the more sophisticated strategy on the competition and isolated own segmentation will probably be necessary in the future.

The product portfolio is summarized in Table 3 on their 3 products in terms of the introduction contacts of basic research findings, targeted market segments, and progress state of product development.

Table 3 J-TEC's Regenerative Medicine Product Portfolio

	Autologous Cultured Epidermis	Autologous Cultured Chondrocytes	Autologous Cultured Corneal Epithelium
Basic Research Partners (for in-license)	1)Prof. M. Ueda, Nagoya Univ.(from founding) 2)Prof. H. Green,Harvard Univ.(May 2008, as an advisor)	Prof. M. Ochi, Hiroshima Univ. (May 2004, start of clinical trial)	Dr. M. De Luca, Univ. of Modena& Dr.G. Pellegrini, Veneto Eye Bank Foundation (August 2003, technology introduction)
Indications	Sever Burn	Cartilage Loss in Knee Joint	Chemical Injury, Burn, Stevens-Johnson Syndrome etc.
Progress Status	Production Approval :October2007 Health Insurance Adaption: January 2009	Submission for Production Approval: August 2009	Submission for Confirmative Application: May 2007
Product Appearance			

(Data: J-TEC home page, business contents, 2011)

And the product pipeline is also shown as Figure 6. It is necessary to intermittently launch and promote next projects according to the development progress of each project in the product candidates. That is, the very dynamic management is required; because it is necessary to put on track manufacturing and logistics in addition to clearing clinical trials, recruiting, and training while collecting and accumulating technologies and monitoring revenues.

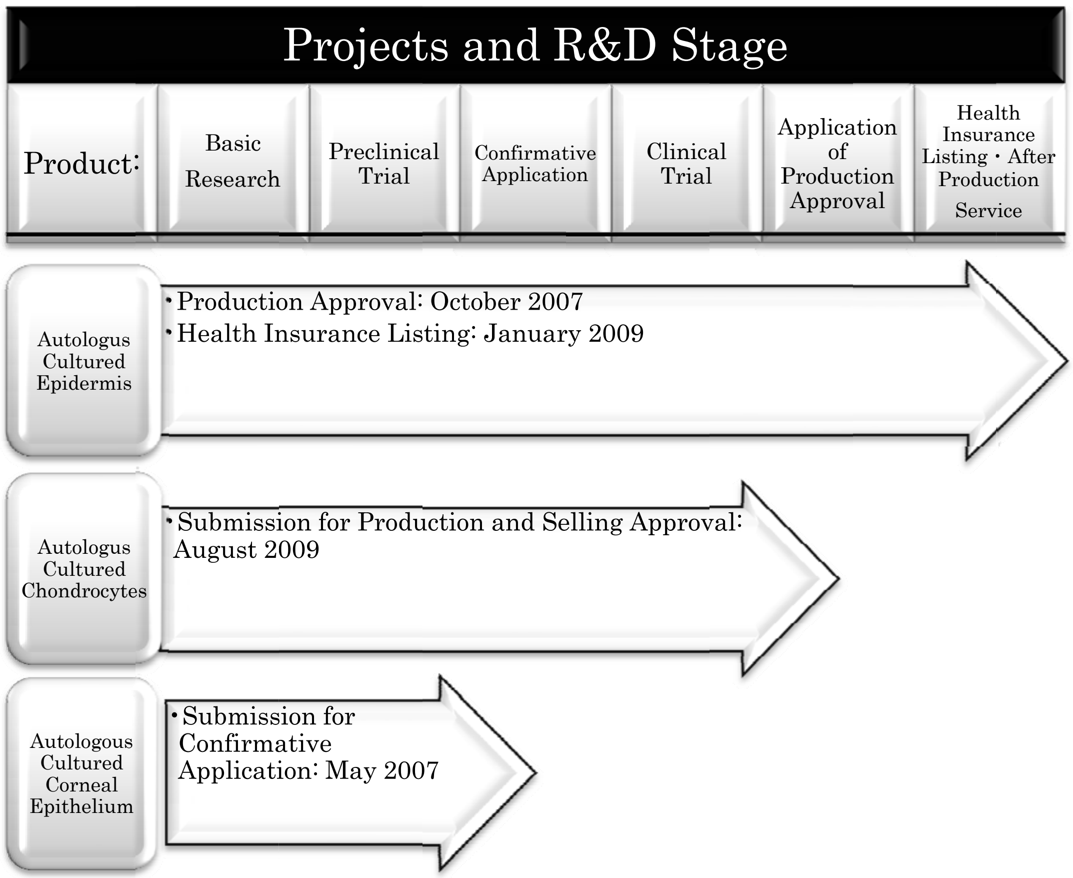


Figure 6 J-TEC's Regenerative Medicinal Product Pipeline (Data: J-TEC home page, 2011)

This company is a biotech start-up in the regenerative medicine related with widely noticed iPS cell that develops products for tissue engineering at long-term valley of deficit, but not in drug discovery. One of robust factors for such valley of deficit may come from relationship with parent company, Nidek. Since as of March 2011, they have 106 employees, not only capital but also recruiting and training are going well. At the success case of OncoTherapy Science from strategic partnerships based on out-license with Otsuka Pharmaceutical and Shionogi, in spite of drug discovery spin-off from University of Tokyo, OncoTherapy Science could turn operating cash flow from negative to positive values from the period of March 2009. Then it may be some room for business expansion in manufacturing and selling through strategic partnership with big healthcare companies, in addition to present business model of self-managed cell culture and delivery within regulation. In spite of difference from drug discovery, since present time needs effective business model of investment for new technologies like genomics for personalized medicine, focus shift from medical treatment to prevention, and healthcare financial sustainability for health insurance and pension, this company's strategy needs to be continually noticed.

At next section, we wish to touch on a tool of stochastic optimization using Monte Carlo simulation from a point of risk and return, for selecting the product candidates for pipeline portfolio.

4. STOCHASTIC OPTIMIZATION

Here we try to apply the method of stochastic optimization for project selection, to enhancement of product portfolio for product pipeline from the relationship between risks and return (Mun, 2006). I used the Crystal Ball as simulation software.

4-1. Assumption for Simulation

As the assumptions of Monte Carlo simulation, the expected NPV, the necessary investment money amount, and the coefficient of variation of 15 projects as product portfolio are set as Figure 7. When putting the values of parameters into each expected value of the NPV and coefficient of variation, following normal distribution is assumed so that each standard deviation is 10% of the expected value. And for stochastic optimization using Monte Carlo simulation, let object function as maximization of Sharpe ratio as risk price, and two constraint functions: one is that the upper limit of investment equal to 7 billion Japanese yens, and the other is that the selected number of project equal or more than nine in 15 candidates.

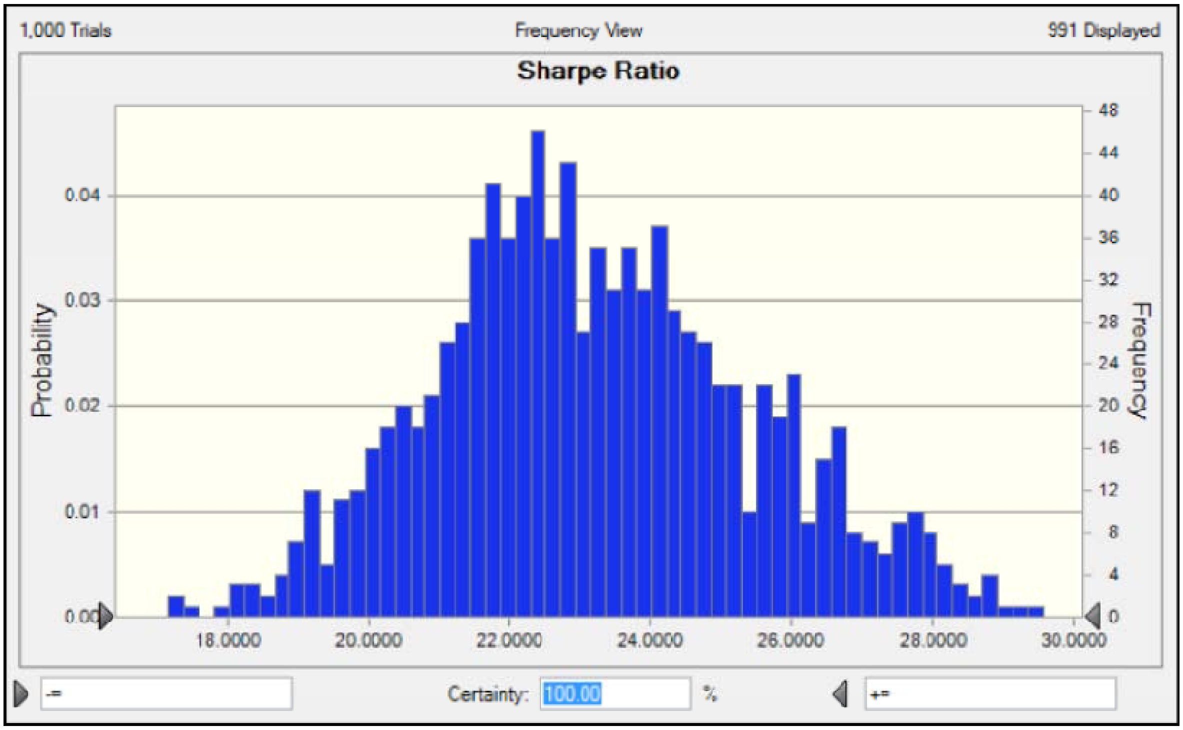
Pipeline	ENPV(¥M)	Investment (¥M)	Risk (¥M)	Risk %	Return to Risk Ratio	Profitability Index	Selection
Project 01	229	1,012	112	49.00%	2.04	1.23	1.0000
Project 02	977	1,074	1,197	122.50%	0.82	1.91	1.0000
Project 03	800	156	600	75.00%	1.33	6.13	1.0000
Project 04	1,126	2,056	450	40.00%	2.50	1.55	1.0000
Project 05	425	573	579	136.25%	0.73	1.74	1.0000
Project 06	758	65	701	92.50%	1.08	12.66	1.0000
Project 07	2,845	948	7,041	247.50%	0.40	4.00	1.0000
Project 08	1,237	144	1,160	93.75%	1.07	9.59	1.0000
Project 09	1,945	2,306	1,653	85.00%	1.18	1.84	1.0000
Project 10	2,250	573	2,391	106.25%	0.94	4.93	1.0000
Project 11	379	56	379	100.00%	1.00	7.77	1.0000
Project 12	525	131	387	73.75%	1.36	5.01	1.0000
Project 13	1,685	875	2,443	145.00%	0.69	2.93	1.0000
Project 14	2,573	2,166	5,583	217.00%	0.46	2.19	1.0000
Project 15	1,264	752	2,086	165.00%	0.61	2.68	1.0000
Total	19,018	12,887	6,643	34.93%			15
Goal:	MAX	< 7,000					>=9
Sharpe Ratio	2.8628						

ENPV=the expected NPV of each project,
Investment =the total cost of administration as well as required capital holdings , and
Risk(%) = the Coefficient of Variation(σ / μ) of the project's ENPV.

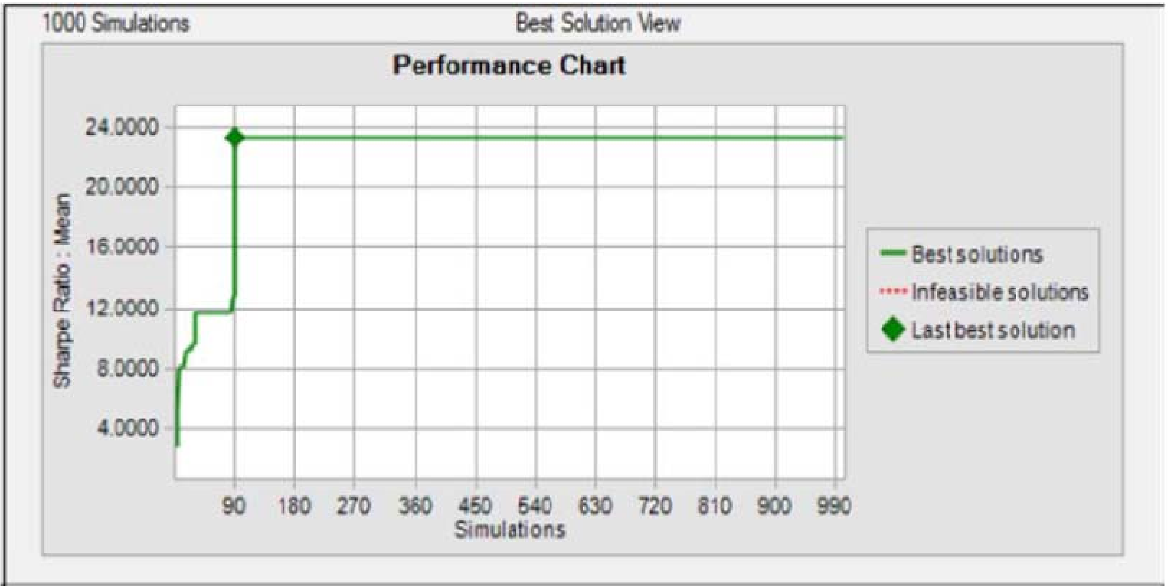
Figure 7 Project Assumptions before Simulation Analysis

4-2. Calculated Results

After 1000 times run of simulation for stochasticoptimization, the Sharpe ratio had the distribution shown as Figure 8 and the maximized value as 23.2. As the calculated results, while selected projects as pipeline candidates were shown as numerical value 1, projects to be postponed were shown as numerical value 0 respectively.



Fiigure 8 Sharpe Ratio Analysis's Distribution



Best Solution:

Objectives	Value
Maximize the Mean of Sharpe Ratio	23.2603

Requirements	Value

Constraints	Left Side		Right Side
Total cost <= 7,000.	6591	<=	7000
Project number >=9	9	>=	9

Decision Variables	Value

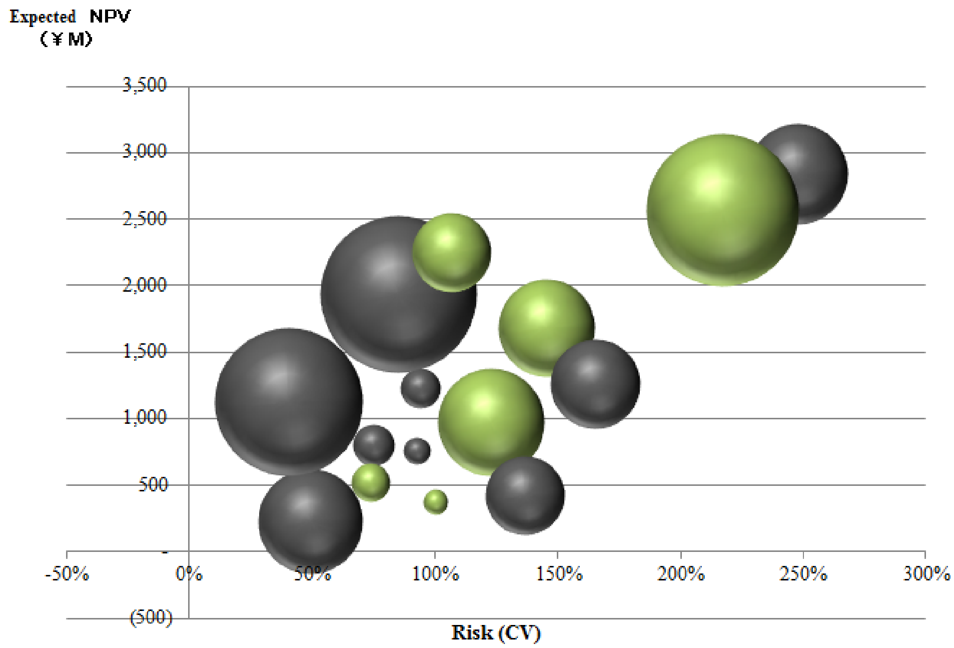
Figure 9 Calculated Results of Stochstic Optimization (1)

Decision Variables	Value
Project #01	1.0000
Project #02	0.0000
Project #03	0.0000
Project #04	0.0000
Project #05	0.0000
Project #06	1.0000
Project #07	1.0000
Project #08	1.0000
Project #09	1.0000
Project #10	1.0000
Project #11	1.0000
Project #12	1.0000
Project #13	0.0000
Project #14	0.0000
Project #15	1.0000

Figure 10 Calculated Results of Stochstic Optimization (2)

4.3 Analysis of Calculated Results

In a plane with the horizontal axis of the coefficient of variation as risk scale and the vertical axis of the expected NPV as expected return scale, if showing the invested money amount as bubble size, each project can be located as Figure 11. Here black bubbles are chosen by this calculation. It can be understood that an efficient frontier as the envelop curve covering each position with larger slope is selected subject to both the budget ceiling and the selection number.



(Bubblle Size = Investment Financial Amount; Black Bubbles = Selection Candiates)
Figure 11 Product Portfolio and Pipeline Candidates

In practice, along with the efficinet frontier, it becomes necessary to do sensitivity analysis on constraints change of the project selection number and the budget limit and further to qualitatively coordinate projects from a strategic point of view.

5. CONCLUSION

In this paper, we examined the characteristics of decision retaining option, in the functions of flexibility of real options including switching options, for overcoming the valley of deficit after financial crisis. And we also studied the case of a biotech start-up in regenerative medicine, J-TEC, from a perspective of robustness against the deficit valley. Further, we applied the stochastic optimization to selecting candidates for product portfolio.

Although traditionally the decision retaining has been discussed mainly from a perspective of sunk cost, the weight of growth option is very important for biotech start-ups in deficit. And R&D is considered as having a decision retaining function as a learning option in itself. Further, for enhancing the robustness against the deficit valley, the enrichment of product portfolio is constantly required. As a managerial tool, the stochastic optimization is possible to use for rapidly selecting project candidates as integer number subject to budgets so on for the efficient frontier.

However, in the future, the relationship between the growth option value and the growth rate of project value must be studied for coordinating trigger prices of entry and exit. And the repeated information asymmetric games in development competition also must be considered for more realistic decisions.

ACKNOWLEDGMENT

This study is supported with Grant-in-Aid for Scientific Research (B) #21330090 by Japan Society for the Promotion of Science.

REFERENCES

(1) Burrill& Company (2009) *Biotech 2009*, San Francisco, C.A.
(2) Burrill& Company (2010) *Biotech 2010*, San Francisco, C.A.
(3) Copeland, T. (2001) *Real Options*, Texere, New York, N.Y.
(4) Dixit, A. (1989) Entry and Exit Decisions under Uncertainty, *Journal of Political Economy*, pp. 620-638.
(5) Dixit A.K. & Pindyck, R.S.(1994) *Investment under Uncertainty*, Princeton Univ. Press, Princeton, N.J.
(6) Fujiwara, T., (2008a) Japan's Health-care Service Quality and the Death-Valley Strategy of Biotech Start-ups, *Global Journal of Flexible Systems Management*, Vol.9 (No.1), pp.1-10.
(7) Fujiwara, T. (2008b) Modeling of Strategic Partnership of Biotechnological Start-up by Option-game: Aiming at Optimization between Flexibility and Commitment, *Journal of Advances in Management Research*, Vol.5 (No.1),pp.28-45.
(8) Fujiwara, T. (2010) Application of Real Options Analysis for Biotech-cluster Formation: Optimal Investment Timing of Biotech Start-ups under Uncertainty, in C. Jayachandran et al., ed., *Business Clusters: Partnering for Strategic Advantage*, Routledge, New Delhi, pp.193-215.
(9) J-TEC (2011)the company home page: http://www.jpte.co.jp/english/
(10)Mun, J. (2006) *Modeling Risk*, Wiley, Hoboken, N.J.
(11) Smith, R.L. et al. (2004) *Entrepreneurial Finance*, 2nd ed., Wiley, Hoboken, N.J.