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Real Options Analysis on Strategic Partnership Dealing of Biotech Start-ups

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Abstract

Biotech start-ups have competitive advantages of quick and efficient combing between the innovative technologies and the niche markets. However they are facing with the short-term financial fluctuations from venture capital and IPO markets after this financial crisis, even if continuing the long-term R&D. Thus strategic partnerships are becoming main fundraising sources. Then, how can such small start-ups optimally negotiate their deal-structures with more powerful big pharmaceuticals companies? This paper discuss about the opportunities and challenges of Monte Carlo simulation for cash-flow forecasting of R&D investment, the sequential compound option for risk-hedge, and the stochastic optimization for negotiating the portfolio of license-fee elements.

Introduction

As research background, the amount of 60.7% in basic research budget has been invested in the life science field in the USA (National Science Board, 2010). As many big pharmaceuticals companies have the problems of patent cliff of blockbuster drugs, they are aggressively not only doing the M&A (Merger & Acquisition) between them but also acquiring biotech start-ups for technology introduction. Their product development target is rapidly changing from chemosynthesis drugs to biopharmaceuticals drugs. And they are shifting more R&D resources from their basic research stage into clinical development as their drug development later stage and tend to often distribute about 50 % of their R&D resources to their outside like biotech start-ups and universities. Further their partnerships in both R&D and clinical stages are increasing even in emerging countries. Thus for biotech start-ups being difficult to access to venture capital and IPO capital markets after Lehman Shock, their strategic partnerships with big pharmaceuticals companies keep the share 66% in biotech start-ups' fund raising since the reasons of high risk, long time to build, and severe resource constrains in 2009 (Burrill, 2010).

As research question, there are 1500 biotech start-ups, of that 310 are public companies in the USA. It has been the first positive average profits of the biotech industry in 2008 since Genentech founding in 1976. However since public companies have only 21.5 % of cash equitable assets, the level of growth option in the company value is still high, depend on the potential for future. The typical biotech start-ups are trying to develop the innovative technology as *nucleic acid drugs for expanding indications from the niche markets as orphan drugs, at the middle stage between the basic research at universities and the commercialization at pharmaceuticals companies. How can they make strategically decisions on the deal structure of strategic partnerships by quantitatively, instead of the relative comparison with similar trades or the*

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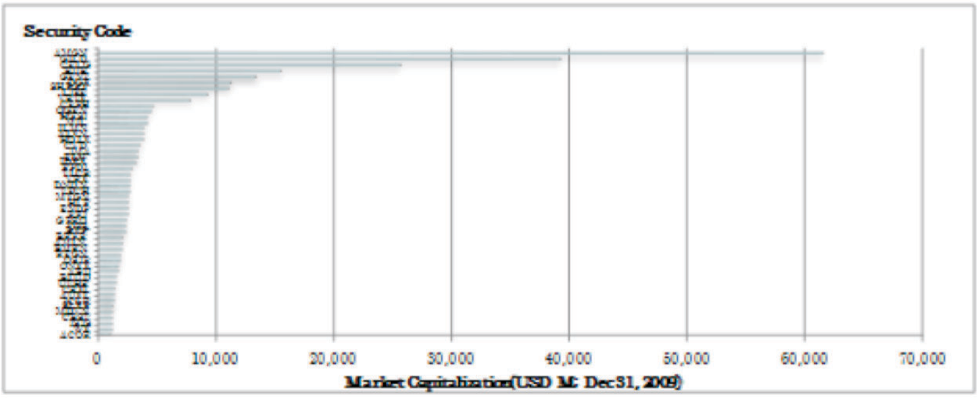
subjective evaluation of business developers?

As the key concept, the biotech start-ups that make the irreversible investment under uncertainty at the middle stage of commercialization of basic research results are defined as the portfolio of real options based on the business opportunity as entrepreneurs' ideas (Smith, 2004). The methodology for above research question is the real options that apply the concepts of financial derivatives to real assets (Dixit, 1994; Fujiwara, 2011). Then by using this, we examine the potential of the promising but high risk projects based on the asymmetric decision with downside risk hedging and upside opportunity grasping under uncertainty.

Assuming the case of business development at the strategic partnerships between biotech start-ups and big pharmaceuticals companies, the objective of this paper is to examine firstly the improvability of business value by the flexible decision of compound rainbow option as a real options to some uncertain factors including the revenue and the success probabilities, and secondly the stochastic optimization as an optimal decision method for the resource distribution to a specific projects in a portfolio.

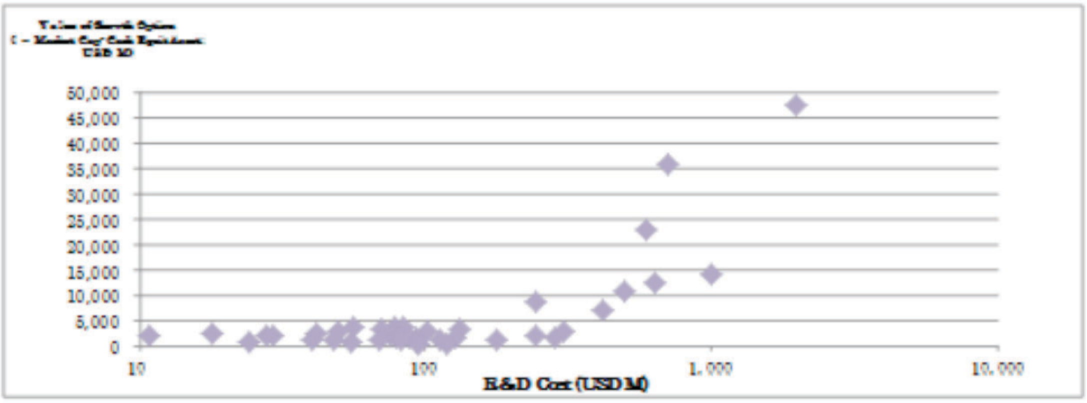
Survival of Biotech Start-Ups and Strategic Partnerships

The distribution of top 50 market capitalization biotech start-ups in the USA is "Pareto Distribution," shown as Figure 1. In 1500 total number of biotech start-ups in the USA, there are 500 public companies. But, except a few decades of the positive profits companies, all of total companies are in the red ink, since it takes more than 10 years for biotech drug discovery start-ups to get an approval for the dug from the US FDA subject to constrained managerial resources. Then only a limited number of biotech start-ups can become the "star" companies.



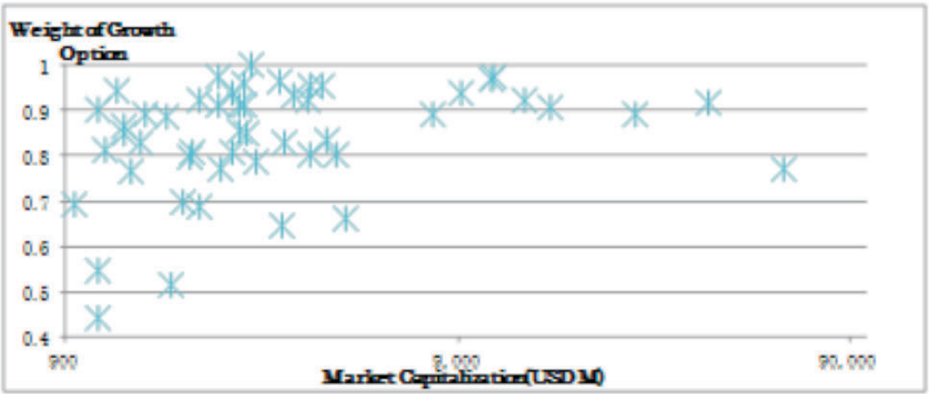
(Data:Burrill, 2010)
Figure 1: The Distribution of USA Biotech Start-ups Top 50 Market Capitalization

In the above group of the US top 50 market-capitalization public biotech companies, there is a jump trend of growth options around the threshold of the $500 million of R&D (Research and Development) Investment level in the plane between R&D Investment as the horizontal axis and Growth Option Value as the vertical axis in 2009 (Figure 2). That is, it means the existence of the time to build or the death-valley for them to endure such severe period to continue theirs R&D without their drugs on the market and positive profits until later mature state.



(Top Market Cap 50; Sep, 2009; Data:Burrill, 2010)
Fugire 2: R&D Investment and Growth Option Value of Biotech Start-ups

The weight of the growth option value to the market capitalization has shown the lower variation and the improving expected value over the increasing level of the market captalization value in the plane between the the market captalization value as the horizontal axis and the weight of the growth option value to the market capitalization as the vertical axis (Figure 3). Then the valuation method is critical for such biotech start-ups to continue their long term R&D during deficti period. But there is the screening or selection process over the market capitalization. Thus at the lower level of market capitalization, the range of the weight is very broad. Following the sceaning on the technological and business potentail, only the more promising cmpnaies can survive and other cmapnies can be reused in recyle loops like refounding after failures and M&A targets.



(Top Market Cap 50th; 2009; Data:Burrill, 2010)
Figure 3: Market Capitalization Level and Weight of Growth Option of Biotech Start-ups

For example, Human Genome Sciences is a success case for placing a drug on the market and then for getting a quantum improvement in the market capitalization. Even if the operating net income had been negative until launching the drug on the market, it was understood for them to maintain the cash flow mainly by the R&D contract revenues with strategic partnerships, and additionally by the corporate bond issues and newly issued stocks (Table 1). Hence, for the biotech start-ups under severe financial conditions, strategic partnerships are very important financial sources.

Table 1: The Financial Data of Human Genome Sciences

HGS Finacial Data (in thousands, except per share and ratio data;Year Ended December 31)

FY	2009	2008	2007	2006	2005	2004	2003	2002	2001	2000
PL:										
Total revenue:	275,749	48,422	41,851	25,755	19,113	3,831	8,168	3,568	12,818	22,068
Product sales	154,074									
Manufacturing and development services	50,653									
Research and development collaborative agreements	71,022	48,422	41,851	25,755	19,113	3,831	8,168	3,568	12,818	22,068
Total costs and expenses	269,561	304,122	298,494	292,126	270,783	270,685	235,091	249,575	184,990	252,589
Cost of product sales	15,805									
Cost of manufacturing and development services	18,215									
Research and development expenses	173,709	243,257	246,293	209,515	228,717	219,549	191,483	205,400	146,276	225,506
Income (loss) from operations	6,188	−255,700	−256,643	−266,371	−251,670	−266,854	−226,923	−246,007	−172,172	−230,521
Net income (loss)	5659	−268,891	−284,371	−264,087	−244,553	−242,898	−185,324	−219,716	−117,152	−243,806
BS:										
Total assets	1,530,630	686,832	949,105	1,149,668	997,046	1,249,385	1,466,204	1,662,187	1,865,004	1,948,525
Current assets	780,768	68,166	173,126	392,049	188,317	743,128	987,979	1,296,916	1,548,398	1,771,598
Cash and cash equivalents	567,667	15,248	34,815	96,942	12,268	24,075	33,269	25,205	88,319	493,867
Property, plant and equipment (net of accumulated depreciatior	263,123	274,315	268,804	285,177	304,809	243,741	154,717	126,437	101,282	38,567
Total liabilities	775,215	823,136	961,007	935,745	580,080	593,338	562,871	561,634	650,541	585,570
Common stock	1,853	1,357	1,349	1,338	1,310	1,305	1,294	1,289	1,283	1,252
Additional paid-in capital	2,932,863	2,059,154	1,866,426	1,836,560	1,786,549	1,775,005	1,762,191	1,757,685	1,753,235	1,698,384
Accumulated other comprehensive income (loss) .	7,365	−4,490	3,152	−3,594	−1,685	9,506	26,719	43,126	31,776	27,998
Accumulated deficit .	−2,186,666	−2,192,325	−1,882,829	−1,620,381	−1,369,208	−1,129,769	−886,871	−701,547	−481,831	−364,679
Total stockholders' equity (deficit)	755,415	−136,304	−11,902	213,923	416,966	656,047	903,333	1,100,553	1,304,463	1,362,955
CF:										
Operating CF	−332	−260,263	−174,659	−146,833	−214,945	−198,901	−171,204	−145,521	−79,629	−104,449
Investing CF	−238,233	239,146	113,166	−21,463	203,573	204,634	251,657	137,417	−217,551	−1,026,199
Financing CF	790,984	1,550	−634	252,970	−435	−14,927	−72,389	−55,010	−108,368	1,443,676
Cash & Equitables:										
Net increase (decrease) in cash and cash equivalents	552,419	−19,567	−62,127	84,674	−11,807	−9,194	8,064	−63,114	−405,548	313,028
Cash and cash equivalents—beginning of year	15,248	34,815	96,942	12,268	24,075	33,269	25,205	88,319	493,867	180,839
Cash and cash equivalents—end of year	567,667	15,248	34,815	96,642	12,268	24,075	33,269	25,205	88,319	493,867

Model Formulation and Monte Carlo Simulation

Model Assumption of the Drug Development at a Biotech Start-up

Here we assume the following biopharmaceutical development project including the net revenues of product selling, and the R&D costs and POS (Probability of Success) from the clinical phase 1. Then let the discount rates as risk adjusted rate is 0.15 and risk free rate is 0.05. After all, the risk-adjusted expected Net Present Value (rNPV) becomes $26 million depending on the POS assumed here.

Table 2: The Assumption of a Biopharmaceutical Development Project

Year	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031
Time Point	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
Net Sales	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$108.1	$138.7	$174.8	$216.0	$266.8	$329.7	$407.4	$503.5	$495.4	$487.4	$479.6	$471.9	$0.0
PV(Net Sales)	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$30.7	$34.3	$37.6	$40.4	$43.4	$46.6	$50.1	$53.8	$46.0	$39.4	$33.7	$28.8	$0.0
R&D costs																						
Phase I	−$1.4	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0													
Phase II	$0.0	−$1.7	−$1.7	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0													
Phase III	$0.0	$0.0	$0.0	−$4.5	−$4.5	−$4.5	$0.0	$0.0	$0.0													
BLA	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	−$0.7	−$0.7	$0.0													
Total Cost	−$1.4	−$1.7	−$1.7	−$4.5	−$4.5	−$4.5	−$0.7	−$0.7	$0.0													
PV(Total Cost)	−$1.4	−$1.6	−$1.6	−$3.9	−$3.7	−$3.5	−$0.5	−$0.5	$0.0													
POS																						
Phase I		56%																				
Phase II				36%																		
Phase III							43%															
FDA Approval									74%													
Cum. Prob.	100%	56%	56%	20%	20%	20%	9%	9%	6.4%													

(USD Million)

Monte Carlo Simulation

On the market growth, competition, and market share of the product sales, and on the cost and POS of the R&D, the Monte Carlo simulation can be applied based on the assumption close to the real situation by using the software, Crystal Ball. Thus, we had each rPV (risk adjusted Present Value) distribution of the Net Sales and the R&D costs (Figure 4, 5). The NPV can be calculated from these two accounts. Then it can be found that while the expected value is equal to $26 million, the rNPV has not only negative but also long positive tail (Figure 6). That is, there are the large promising chances as well as the risks.

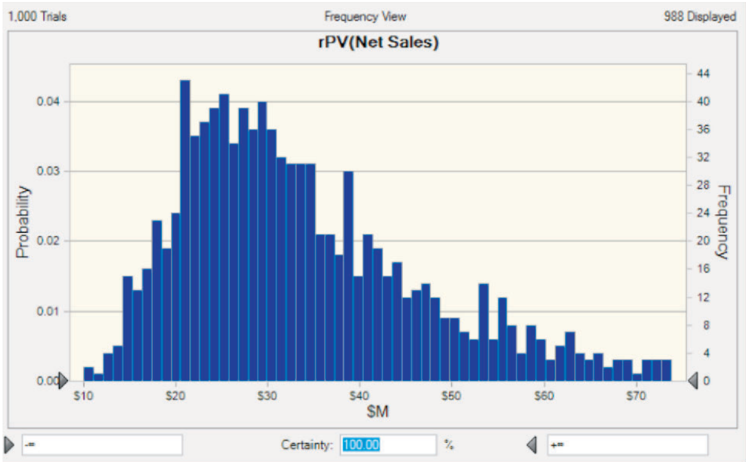


Figure 4: The Simulated Distribution of Risk Adjusted Present Value of Net Sales

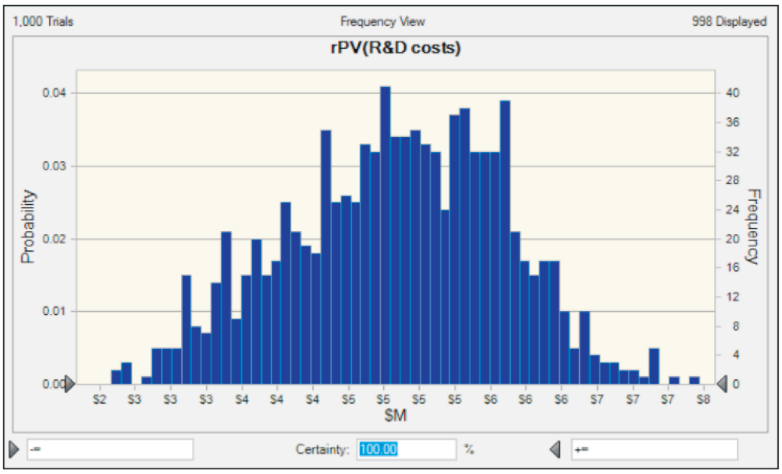


Figure 5: The Simulated Distribution of Risk Adjusted Present Value of R&D C

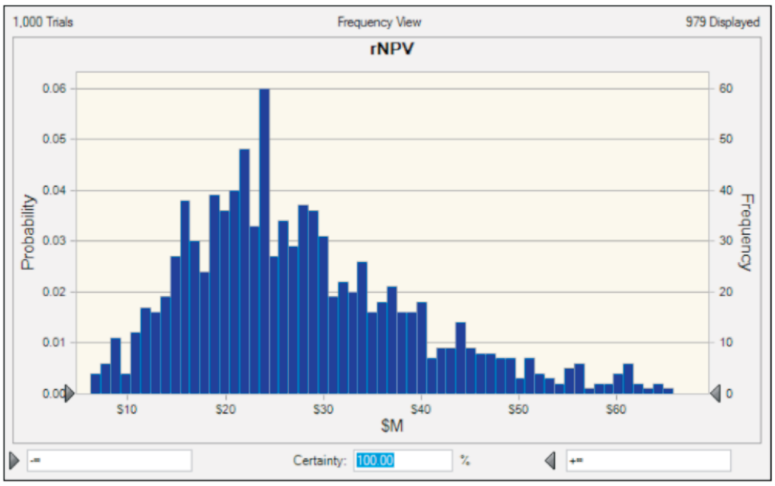


Figure 6: The Simulated Distribution of Risk Adjusted Net Present Value

Business Development of Strategic Partnerships

For the survival method for biotech start-ups, we assume the *Strategic Partnership* for this biopharmaceutical development project between a biotech start-up and a big pharmaceuticals company. Let the partnership deal of license agreement be after clinical phase 1, the R&D stage be done by the biotech start-ups, and the stage after manufacturing be done by the big pharmaceuticals company. The basic agreement points are supposed as firstly the R&D funding: the clinical phase 1, annual $1.4 million; phase 2, $1.7 million; phase 3, $4.5 million, and BLA (Biologic License Application), $0.7 million, secondly, the up front payment, $5.0 million, thirdly the milestone payments: phase 1, $8 million; phase 2, $10 million; phase 3, $50 million; and FDA (Food and Drug Administration) approval, $100 million, and fourthly the royalty, 11% for product sales, each paying to the biotech start-ups from the big pharmaceuticals company.

And let distribute 60% to the manufacturing cost and 5% to the primary license fee to a university respectively from the sales.

License Fees

After the Monte Carlo simulation based on the above assumptions, the distribution of the up front and the milestone payments depending on timing has the large dispersion, then not only upside chances but also high risk for revues (Figure 7). While the R&D funding does not have so large financial amount, it is close to the normal distribution and then regarded as the fundamental earnings (Figure 8). And the royalty has the large financial amount, but the distribution is close to the lognormal distribution (Figure 9). Then it means high volatility for revenues.

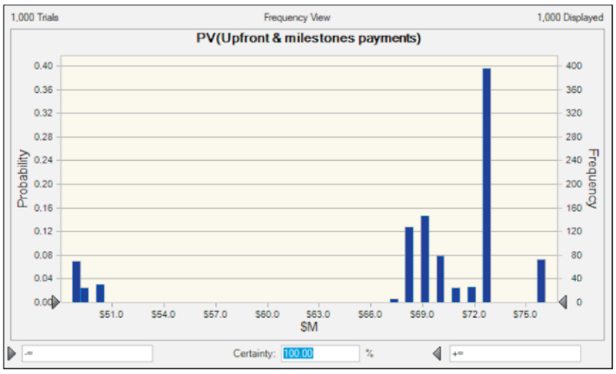
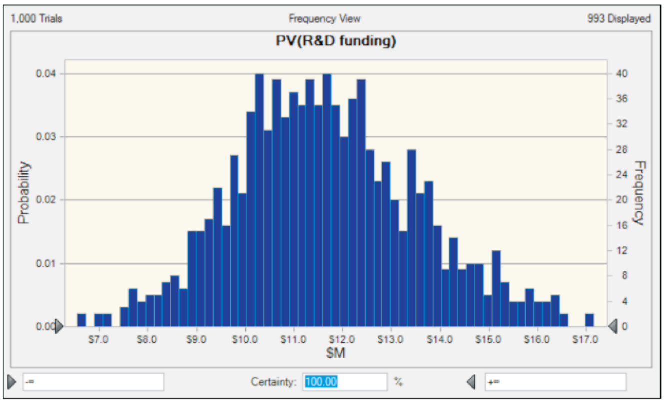


Figure 7: The Simulated Present Values of the Up Front and the Milestone Payments



Fugure 8: The Simulated Present Value of R&D Funding

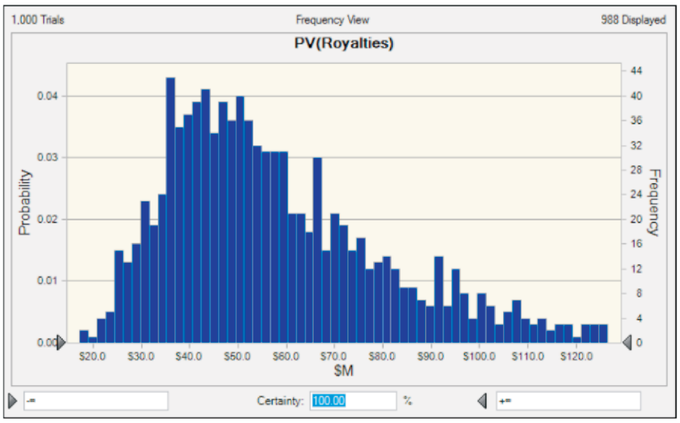


Figure 9: The Simulated Present Value of Royalty

Biotech Start-ups

From this partnership assumed here, the revenue of biotech start-up is come from the license fees consisted of the R&D funding, the up front, the milestone, and the royalty those that have already been seen (Figure 10). The main cost is the R&D cost invested inside the company and around $16 million (Figure 11). Then the NPV as the difference between the revenue and the R&D cost can be expected as Figure 12. That is, the achieving range from $90 million to $170 million of the NPV is forecasted as the probability 90% by this simulation.

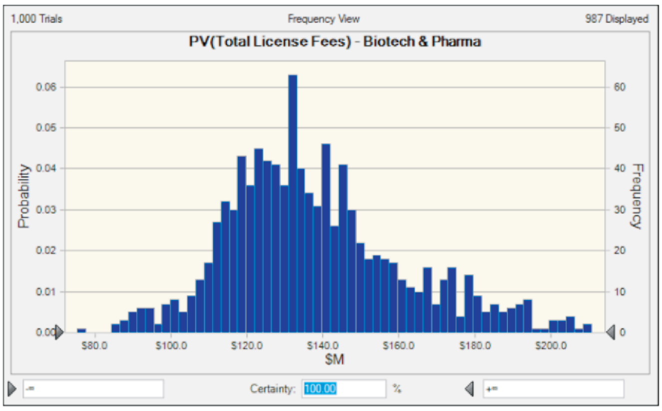


Figure 10: The Simulated Present Value of Total License Fees

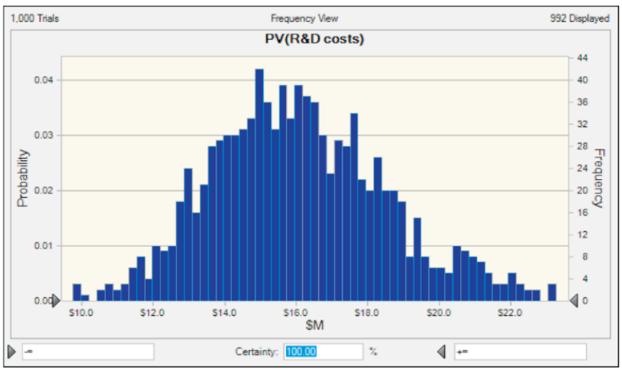


Figure 11: The Simulated Present Value of R&D Costs

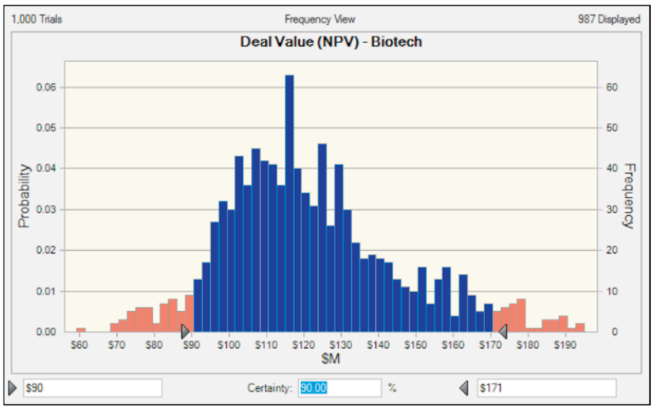


Figure 12: The Simulated Net Present Value of the Biotech Start-up

Big Pharmaceuticals Company

On the other hand, at this strategic partnership, the NPV of the big pharmaceuticals company is calculated by the net sales (revenue, Figure 13) minus the license fees (the revenue for the biotech start-up). The NPV range of the big pharmaceuticals company is from $153 million to $775 million in the probability of 90% (Figure 14). And the basic statistical results of this simulation include the expected value, $386 million, and the standard deviation, $194 million. Then this expected value of this NPV is used for real options analysis in next section (Table 3).

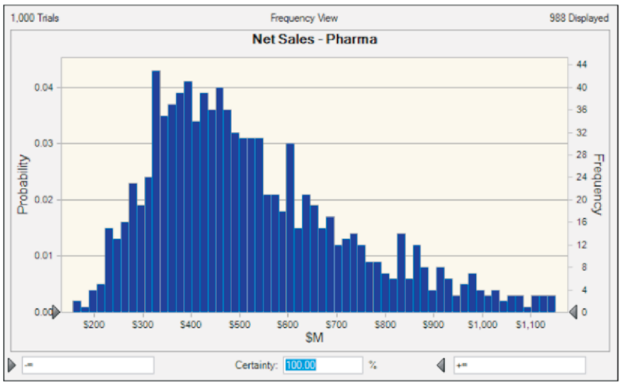


Figure 14: The Simulated Deal Value (Net Present Value) of the Big Pharmaceuticals Company

Table 3: The Statistical Data of the Net Present Value of the Big Pharmaceuticals Company

Statistic	Forecast values
Trials	1,000
Base Case	$346
Mean	$386
Median	$345
Mode	---
Standard Deviation	$194
Variance	$37,571
Skewness	1.67
Kurtosis	7.54
Coeff. of Variability	0.5028
Minimum	$68
Maximum	$1,537
Mean Std. Error	$6

Real Options Analysis and Stochastic Optimization

Real Options Analysis

Here, we examine the effectiveness of real options alanysis to this partnershisp deal. I applied the rainbow sequestial comound option by considearing the risk hedge function at each development stage and the multuple fluctuationable risks including the technological development success rate and product market value risk (Figure 15). Since later more broad range of the flexible decision opportunities, from the perspective of the big pharmaceuticals company, the option value created is $14 million by calculating the expanded NPV(from the flexible decision), $423 million minus the NPV (the benchamrk from revious section), $386 million. Thus this milestone type of R&D partnership deal can create the flexibility value, $14 million in itself.

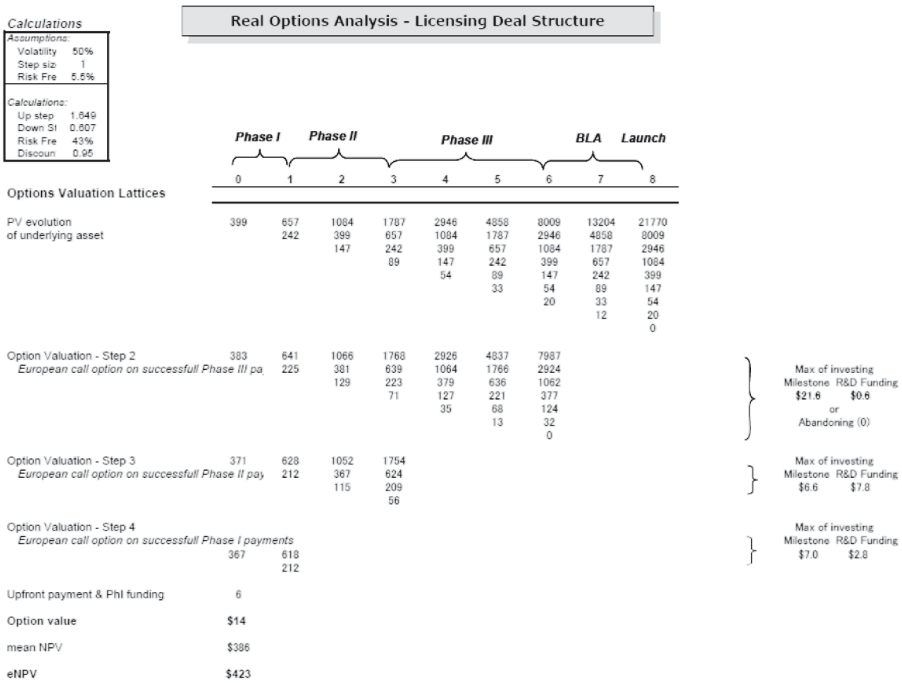


Figure 15: Real Options Analysis on Strategic Partnership Deal

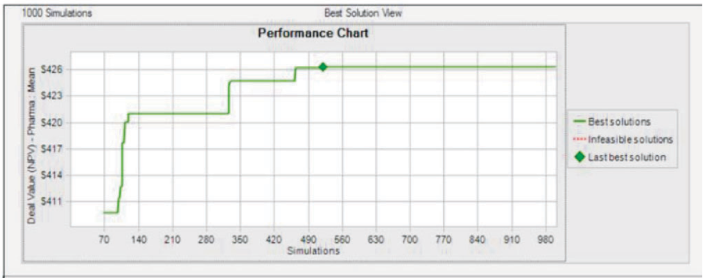
Stochastic Partnership

Here I tried the stochastic optimization of each expected NPV by decision variables of license fee elements subject to a few constrains as the resources or each counterpart NPV. For the big pharmaceuticals company, subject to the maximum of total license fees, $120 million, and the minimum NPV of the biotech start-up, $85 million, the expected NPV as objective function stochastically optimized is $426 million, with decision variables as the up front, $3.0 million, the milestone phase 1, $5.0 million, the phase 2, $5.0 million, the phase 3, $40.0 million, the FDA approval, $50.0 million, R&D funding 76.9%, and the royalty, 7.0% respectively after 1000 simulation runs (Figure 16).

On the other hand, for the biotech start-up, subject to the minimum PV of R&D cost payment, $10 million, and the minimum NPV of the big pharmaceuticals company, $250 million, the expected NPV stochastically optimized is $392 million, with decision variables as the up front,

$100.0 million, the milestone phase 1, $5.0 million, the phase 2, $8.0 million, the phase 3, $20.0 million, the FDA approval, $89.0 million, R&D funding 100.0%, and the royalty, 48.0% respectively after 1000 simulation runs (Figure 17).

There are some negotiation opportunities available between the above gaps of each decision variable.



Best Solution:

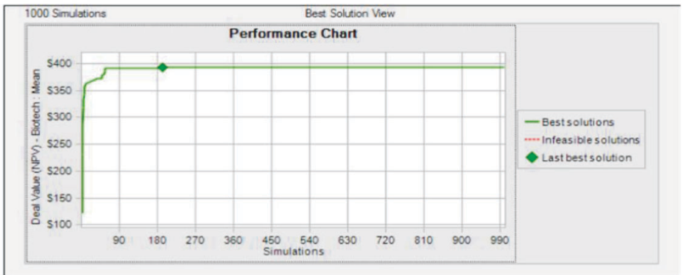
Objectives	Value
Maximize the Mean of Deal Value (NPV) - Pharma	$426

Requirements	Value

Constraints	Left Side		Right Side
'RA Deal Term Scenarios (2)'!F47 <= 120	101.459738048604	<=	120
'RA Deal Term Scenarios (2)'!F51 >= 85	85.5373695027285	>=	85

Decision Variables	Value
FDA Approval	$50.0
R&D Funding	76.9%
Royalties (net sales)	7.0%
Successful PhI	$5.0
Successful PhII	$5.0
Successful PhIII	$40.0
Upfront payment	$3.0

Figure 16: Stochastic Optimization of the NPV of the Big Pharmaceuticals Company



Best Solution:

Objectives	Value
Maximize the Mean of Deal Value (NPV) - Biotech	$392

Requirements	Value

Constraints	Left Side		Right Side
'RA Deal Term Scenarios (2)'!F49 <= -10	-15.9223685458751	<=	-10
'RA Deal Term Scenarios (2)'!F35 >= 250	250.136981944749	>=	250

Decision Variables	Value
FDA Approval	$89.0
R&D Funding	100.0%
Royalties (net sales)	48.0%
Successful PhI	$5.0
Successful PhII	$8.0
Successful PhIII	$20.0
Upfront payment	$100.0

Figure 17: Stochastic Optimization of the NPV of the Biotech Start-up

Conclusion

Hence biotech start-ups need to build the business model based on the strategic partnerships between the universities and the pharmaceuticals companies for the commercialization of life science. At the time, it is possible to utilize the decision making tools as the real options and the stochastic optimization for the irreversible investment under uncertainty. For future research, I wish to examine the building possibility of more ideal win-win relationships from the perspective of game theory.

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