The Value of Pharmaceutical R&D Projects under Uncertainty and Drug Approval Policy

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Abstract

Pharmaceutical R&D projects often have the characteristics of irreversibility on investment, flexibility of investment timing, and uncertainty in cash flows. In this thesis, the real options approach is used as the evaluation tool for these projects and three continuous-time investment models are developed. In chapter 4, we discuss the effects of the investment lag and commercialization flexibility on the investment decisions under uncertainty. Chapter 5 examines which organizational structures, the decentralized or centralized pharmaceutical R&D project, are more socially desirable in terms of early investment and higher project value. Chapter 6 considers whether adding a time constraint on the drug development process will increase the investment incentives and how remuneration level will influence the quality of the products, as well as the timing of commercialization.

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Declaration

I declare that except where specific reference is made to the work of others, the contents of this dissertation are original and have not been submitted in whole or in part for consideration for any other degree or qualification in this, or any other university. This dissertation is my own work and contains nothing which is the outcome of work done in collaboration with others, except my supervisor Professor Jacco Thijssen. Chapter 4 and 5 of the thesis are joint work with Professor Jacco Thijssen and Chapter 6 is an independent work. All sources are acknowledged as references.

Chapter 1

Introduction

1.1 Motivation and the Problems Solved in the Thesis

The pharmaceutical industry is an indispensable part of modern society since it plays an important role in improving peoples' health and the quality of their lives. Researchers have exerted great efforts in solving many of the problems in the industry such as making policies to increase investment incentives for research and development (R&D) projects in order to tackle the neglected diseases by setting reasonable quality standards for drugs so that patients will benefit from its therapeutic improvements. Meanwhile, investors would not be intimidated by the unattainable quality level and reject the investment proposals. Although there are usually no quick fixes to these problems, every effort towards perfection, no matter how small, is important and so I am motivated to study, practice and help solve these problems.

This thesis will discuss the various problems concerning the different phases of the R&D process. There are usually three essential phases before the launch of a new drug: the discovery or pre-clinical phase, R&D, and commercialization. The combination of the three phases of clinical trials is referred to as the R&D process. In the discovery phase, animal testing is conducted and the results are crucial in

determining whether they are safe enough for human testing. If sufficient evidence suggests that the drugs are safe for human testing, a sequence of clinical trials will begin. Usually, three phases of clinical trials will be conducted to make sure that the new chemical entities (NCE) will advance to the new drug application stage where the authority decides whether to approve the drug or not. Finally, if the product is proven successful by the authority, the commercialization process starts and at this stage, revenue is generated.

In chapter 4, this thesis will introduce the concept of commercialization flexibility. Commercialization flexibility allows the decision maker of any R&D project to delay selling the drugs by the end of the R&D phase when they are approved. On the other hand, if there is no commercialization flexibility, commercialization is immediate, giving the decision maker no choice but to launch selling the products at the approval date.

In an R&D project with commercialization flexibility, two decisions are considered: when to optimally start the R&D process and when to optimally start the commercialization process. Both of these processes should be considered simultaneously; therefore, the decision maker's problem can be viewed as a compound option. However with projects with immediate commercialization, there is only one decision to be made: when to optimally start the R&D process. This thesis will discuss the effect that commercialization flexibility has on the projects that are suitable for accelerated approval and priority review.

In 1992 and 2014, the US Food and Drug Administration (FDA) and Medicines & Healthcare Products Regulatory Agency (MHRA) in the United Kingdom launched the "FDA Accelerated Approval Program" and the "Early Access to Medicines Scheme" (EAMS) respectively, to facilitate and expedite development and review of new drugs, in order to address unmet medical needs in the treatments of any serious or life threatening conditions. A serious disease or condition is defined in the expanded access regulations as follows:

> . . . a disease or condition associated with morbidity that has substantial impact on day-to-day functioning. Short-lived and

> self-limiting morbidity will usually not be sufficient, but the morbidity need not be irreversible if it is persistent or recurrent. Whether a disease or condition is serious is a matter of clinical judgment, based on its impact on such factors as survival, day-to-day functioning, or the likelihood that the disease, if left untreated, will progress from a less severe condition to a more serious one.[1] (Page.2)

Both programs aim to ensure the therapies of the above conditions are approved and available to patients as soon as possible if the therapies' benefits justify the risks. However, from the perspective of the pharmaceutical companies, it is unclear whether immediate commercialization on the approval date is an optimal strategy. Therefore, the influence that commercial flexibility will have on investment incentives is worth discussing.

Before going deep into the problem, it is ideal to think of two possible scenarios. The first is that commercialization flexibility is allowed and the decision maker has the option to defer selling the products by the end of the R&D process. The policy offers more flexible options that are favorable to the investors such that investment incentives are increased and the projects will be started sooner. However, the flexibility may also delay the commercialization process. The second scenario is that commercialization flexibility is not allowed and pharmaceutical companies are compelled to sell the products immediately on the approval date. This policy will decrease the investment incentives so that projects will be started later. However, since no commercialization flexibility is allowed, the products will be available to the patients by the end of the R&D process.

In these two scenarios, it is not clear which project will allow patients to have earlier access to the products. Moreover, it is controversial whether commercialization flexibility will always increase investment incentives and thus lead to earlier investments under uncertainty since uncertainty allows the decision maker to wait

[1] http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM358301.pdf

longer to avoid the risks and invest only if the conditions are favorable enough. This type of event is usually considered as the "bad news principle".

In this chapter, this thesis will discuss which project, with or without commercialization flexibility, provides more investment incentives causing faster investments; and whether commercialization flexibility will prolong or shorten the time that the final products are launched in the market.

In chapter 5, this thesis considers how structural arrangements, private, public or private-public partnerships for pharmaceutical R&D projects may address the lack of investment issue on tackling Neglected Tropical Diseases (NTDs). Since the main reason for lack of investments lies in the uncertainty of a future market, public organizations could help ease the problem by signing the Advance Purchase Commitments (APC) contract in a private-public partnership (PPP).

Is it possible to infer that the problem will be less severe if the government takes more responsibilities? Dependent on the participation degree of the government in the projects, free market is, at one extreme, where no public sectors are involved. A social planner's project, which is conducted solely by the government, is at the other extreme. The project with private-public partnership or the decentralized project is between the two extremes. This thesis will focus on the decentralized project and the social planner's project since free market does not provide a good solution to the lack of investment problem.

In comparison of the projects, three problems are discussed. The first problem is which project, when decisions are optimally made to maximize the project values, will start sooner. For the products with the same required standards of quality, one could expect that an earlier start of the project means a faster finish granting patients earlier access to the potential treatments. To figure out the investment timing of both projects, the optimal investment thresholds will be compared. A lower investment threshold implies earlier investment timing.

Second, we analyze how remuneration levels can be used to adjust the standards of quality of the products. Despite the importance of incentivizing pharmaceutical companies to invest in drug developments and to start the project sooner, making

sure that the products have a high standard of quality is also of great concern. In this model, a noticeable difference between the decentralized project and the social planner's project is that the decentralized project is a game with two players, the government and a pharmaceutical company, while in the social planner's project, the pharmaceutical company is not involved and only the government will be in charge of the whole project. Thus the remuneration level will need to be considered in the decentralized project while and not within the social planner's project. In addition, the remuneration is considered to be the revenue for the pharmaceutical company but costs the government money in the decentralized project. Moreover, it is shown that the remuneration level, which can be used as a great tool of adjustment, can affect the optimal standard of quality. However, this is not feasible in the social planner's project.

Last, the value of the projects, under different managerial structures, is compared. In the decentralized project, it is shown that even if remunerations are internalized by adding the project values of the pharmaceutical company and the government, the total value of the decentralized project is different from the social planner's project. The reason for this difference is that the optimal decisions made in the decentralized project are constrained maximization problems, while the maximization problem is unconstrained in the social planner's project.

In chapter 6, this thesis discusses whether a time-constrained R&D project may help further increase investment incentives in the projects that aim for NTDs in the low-income countries. The purpose of the chapter is to discuss the effects that time constraint will have on the investment incentives in the APC to deal with NTDs. According to WIPO (2005), between 1975 and 2000, it is estimated that only 10% of global R&D resources were directed at diseases accounting for 90% of the global disease burden. Also, in this 25-year period, only 13 new drugs for neglected diseases were approved for use. The primary reason for lack of investment in fighting NTDs is that most of the patients who suffer from these diseases live in low-income countries and the prices of treatments are not affordable to them. In other words, their need for treatments can hardly be turned into demand with

foreseeable profits. Hence it is understandable why few R&D projects are specific to the diseases in these countries.

In addition, free markets alone do not provide with a solution so the involvements of governments, NGOs and philanthropists are crucial since these non-profit driven organizations can be relied upon to provide the market that the pharmaceutical companies need. Among the numerous proposals for stimulating more research with the participations of the above organizations, the Advance Purchase Commitments (APC) contract is claimed to be one of the most effective approaches to increase the incentives of the pharmaceutical companies since it guarantees a solid future market with a legally binding contract (Kremer et al. (2005)).

The outline of the commitments is as follows:
(1) Define a technical specification of the potential product.
(2) Specify the price and quantity that makes the patients affordable and the manufacturers profitable with payments from sponsors.
(3) Manufacturers are obliged to keep providing further treatments at sustainable prices afterwards.

Mostly, there are no constraints regarding when the products have to be finished. The pharmaceutical companies will receive the payments from the sponsors as long as the technical specification is met regardless of how long it takes. Thus the companies do not have incentives to speed up investment. This is less of a problem if the contract is a "winner-take-all" arrangement since companies will have to compete to be the first producer so that they will be awarded. However, in practice, the arrangement of multiple winners is more reasonable because it does not only provide more incentives for manufacturers to join without competition, but it also makes the coexistence of products with varying benefits and risks possible (Berndt and Hurvitz (2005)).

Without setting a deadline of drug development in the contract, the pharmaceutical companies have less incentive to accelerate the developments that are crucial to the patients in serious conditions. A natural solution will be to add a time constraint in the contract specifying when the R&D process should be finished or the rewards

will be reduced dramatically. In this case, the pharmaceutical companies may not finish the projects on time if the projects are not started earlier, which will likely increase their investment incentive. Thus the value of the project will also depend on the time of expiration of the investment opportunity.

It is worth noting that although the thesis is pharmaceutical industry oriented, the models developed in the three chapters are not only applicable to the R&D projects. These models can be used to evaluate any R&D projects that are featured with either the combination of compound options, investment lags and time constraint or with these properties respectively. For instance, an irreversible R&D project to develop a new type of car with both options to decide when to start the R&D process and the flexibility on when to launch the sell of the cars can also be evaluated by using the models in chapter 4.

1.2 The Real Options Approach and its Synergy with Pharmaceutical R&D Projects

In standard economics theories, the rule of thumb to determine whether an investment is worth taking or not is to calculate the Net Present Value (NPV) of the project. The investment proposal is acceptable if the project has a positive NPV, i.e., when the present value of the cash inflow is greater than the present value of the cash outflow. The investment proposal is rejected if the NPV is negative. However, The "NPV rule" does not fit every problem since an NPV calculation only uses information that is known at the time of the appraisal. The decision maker is not allowed to adjust to new information even if more choices are available in the future.

More specifically, if NPV calculation is used in the following conditions, the project value will tend to be underestimated. First, the costs spent to start the project are sunk costs and irreversible. Any improper decisions made can have tremendous impacts on the profitability of these projects. Second, the investment decisions do not have to be made right away. Decision makers then have the flexibility to wait

while updating information and pay the sunk costs only if the situation is favorable enough. Last, the cash flows are uncertain and subject to variations.

It is the "risk-adjusted expected NPV" and not the current NPV that matters. Since the value of the project is affected by both the expected NPV and the discounting effect of time, it is possible that the discount expected NPV of the project in the future is positive while the current NPV is negative. Thus a rejected proposal by the "NPV rule" can be accepted in the context of the real options theory and a project with good potential can be saved. The reason that the NPV rule does not fit for the pharmaceutical R&D projects is that most of these projects are endowed with the above three properties: irreversibility, uncertainty and flexibility.

For irreversibility, according to DiMasi et al. (2016), it is estimated that the average pre-tax cost of new drugs and biologics development is $2,870 million (2013 US dollars), which includes the costs of pre-human research, clinical studies and post-approval research. Although it is common for certain projects to be abandoned during each of the phases, most of the costs spent are irreversible once out of pocket. Furthermore, various types of uncertainties exist in the industry. Among these, technical uncertainties are the greatest one. O'Hagan and Farkas (2009) show that the traditional approach to R&D, which relies on the number of "shots on goal" hoping some lucky result will be obtained, is getting less effective.

The philosophy of this traditional approach is based on the idea that the company will have a better chance to invent a profitable product with more attempts on drug discovery. Also, the reason that taking "shots on goal" matters to R&D is while many of the potential products look very promising in the lab, it is unclear whether they will be translated into effective therapeutic treatments for patients. This typical pattern of coming up with new products leads to great volatility in the expected profits in the industry.

Besides, the uncertainties from the regulators setting new rules for the safety and effectiveness of products, competitors coming into market with alternative brand or generics and disgruntled shareholders also make it difficult to estimate the expected payoffs.

Lastly, because of the numerous uncertainties in the pharmaceutical industry, investors have to think before they leap. Although competitors or shareholders may sometimes exert pressures on earlier adoptions of the investment decision, decision makers are usually provided with the flexibility to wait and keep on updating information until it is optimal to start the R&D process. Because of irreversibility and uncertainty, the value of flexibility can be high. The conclusions drawn on the real options approach in terms of the evaluation and feasibility of projects can be quite different from those using the NPV rule since the value of flexibility is not taken into account in the latter approach. Hence, to make better investment decisions on pharmaceutical R&D projects, the real options approach is chosen in the thesis.

1.3 Contributions

This thesis both contributes to the Health Technology Assessment (HTA) and the Real Options literature. This thesis contributes to the HTA literature by providing possible solutions to solve the lack of investment problem on NTDs in the developing countries. Three models were developed to look at how investment decisions are affected under different scenarios so that possible policies can be made to encourage earlier investments. In each model, we discuss a specific potential policy, such as offering commercialization flexibility after drug approval, altering the managerial structure of the project and exerting time constraints on the development stage, that will probably help ease the problem.

By comparing the benchmark models with the models that policies are implemented, policy recommendations are provided. Moreover, since most of the pharmaceutical R&D projects have the properties of irreversibility, uncertain cash flows and flexible investment timing, the real options approach is used to estimate the value of projects, the optimal investment and commercialization thresholds, and the optimal quality standard of the products that the government sets. In the HTA literature, the mostly widely used approaches to evaluate R&D projects are net present value (NPV), expected net present value (ENPV) and discounted cash

flows (DCF) (Hartmann and Hassan (2006)). Besides, the financial indicators such as return on equity (ROE) and internal rate of return (IRR) are also considered.

However, these approaches are static analyses, which fails to capture the option value and underestimates the project values. When the real options approach is used to evaluate pharmaceutical R&D projects, the three properties mentioned above are carefully taken into account. Thus it suits the evaluation of the pharmaceutical R&D projects better.

This thesis also contributes to the Real Options literature. In chapter 4, it models an R&D project, which combines a compound option with an investment lag. Normally, when a compound option is exercised, the holder of the option will get a new option immediately. However, when an investment lag is combined, the holder no longer acquires the new option at the exercise date, but at the end of the investment lag. Thus the lag makes the value of the new option a random variable at the exercise date. The uncertainty of the value of the new option further complicates the optimal investment decisions.

In chapter 5, this thesis assumes the value of the project is dependent on a stochastic process that has different growth rates before and after the investment taking place, which requires the consideration of different expected discount factors in the optimal stopping problem. This makes the comparison of the project value more difficult when the projects have different optimal investment timings.

In chapter 6, this thesis models the sudden success of a time-constrained R&D project by a Poisson process. It is found that the intensity of the Poisson process λ is of great importance in determining the optimal investment threshold in this model, while λ is usually considered to be a less important parameter, which simply enters the analysis through increasing the discount rates in other models (Hsu and Schwartz (2008)). The impression that the intensity only increases the discount factor can be misleading in particular problems.

In chapters 4 and 5, it is assumed that the projects will be successful with probability 1 and even if the project in chapter 6 has the possibility of failure, the abandonment options are not considered in all the related chapters.

In practice, the abandonment options are particularly crucial to the pharmaceutical industry since the former promising product may result as unpromising as more information is collected during the R&D process. The flexibility of abandonment enables the decision makers to minimize the losses even if the previous investment decision was problematic. Nevertheless, as it has been shown in the real options literature, the abandonment option will usually decrease the option value of waiting since the project is no longer (partly) irreversible, which will often lead to earlier investment. In order to focus on the problems that we are interested in, the abandonment option is not considered during the R&D process in the thesis.

Chapter 2

Literature Review

2.1 Real Options Literature

Following Myers (1977), it is quite natural to think of many investment problems that feature irreversibility, flexibility and uncertainty as real options. According to the classification of Trigeorgis (1993a), there are seven types of real options: to defer, time to build, alter operation scale, abandon, switch, growth and multiple interacting options.

Among all, one of the most common flexibilities on investment is the option to defer. With this option, the decision maker does not have to make the investment decision right away under uncertainty. Instead, he or she can wait while updating information needed to execute and only kill the option when information is favorable enough. Waiting implies both discounting and variation of the future NPV. Since it is possible that the discounted future NPV is larger than the NPV of immediate investment, the option to defer adds value to the whole project. This type of option has been examined in many papers such as Tourinho (1979), McDonald and Siegel (1986) and Majd and Pindyck (1987). Though different investment projects are considered in these papers, the one thing in common is that the the option values are proved to be crucial in calculating the values of these projects.

Another option shown in this thesis is the compound option. Geske (1979) points out that many opportunities have a sequential nature, where latter opportunities are available only if earlier opportunities are undertaken. Also, in the paper of Geske (1979), a theory is presented to price the option to acquire a latter opportunity which depends on financial instruments. Similarly, Carr (1988) discussed a compound option that the latter opportunities are options to exchange for other options. Both papers use contingent claim analysis (CCA) to compute the option values. In chapter 5, we model a pharmaceutical R&D project that has both the options to defer R&D and commercialization process. Moreover, the former option is the prerequisite for having the latter one. Hence the project can be considered as a compound real options. However, dynamic programing, instead of CCA, is used in calculating the option and project values.

In Kulatilaka (1995), it is concluded that a project that has the following characteristics will lead to time-to-build option values: (1) Investment decisions and associated cash outlays occurring sequentially over time; (2) a maximum rate at which outlays and construction can proceed, namely, it takes "time to build"; and (3) a project yielding no cash returns until it is completed. In a sense, the models in this thesis can be considered as simplified versions of time-to-build models.

First, it is assumed in the thesis that the R&D costs are paid as cost flows in some projects. However, it is also assumed that no further decisions will be made during the R&D process and the project will continue to proceed till the end of it without abandonment options. Second, the projects take time to finish. But no variables specifying the speed of construction or outlays are presented. Instead, we either specify a fixed time or under certain rules, such as a jump in the quality standard being reached, that the project will be finished. Thirdly, no revenues are generated until the project is finished which conforms to the second characteristic of a time-to-build model. The time difference between investment costs and payoffs complicates the valuation of a project. On one hand, the payoffs will need to be discounted back to the time when investment costs are paid. The problem of how much value will be discounted is not always easy. On the other hand, uncertainty

increases with time, hence the future expected NPV of projects is extremely volatile. The combination of the two problems increases the difficulty of evaluations.

In real options literature, the duration of time between the start and completion of a project is usually called the investment lag, [1] delivery lag or implementation lag, which has been used to model construction delay in many papers. Alvarez and Keppo (2002) considers a model of investment where investment lag is dependent on the underlying stochastic process. They find that the impact of delivery lag on investment is negative. In other words, an increase in the investment lag delays investment. Sarkar and Zhang (2013) argues that the conventional result "increase in uncertainty and investment lag should have inhibiting effect on investment" can be reversed if the project has sufficient reversibility. Majd and Pindyck (1987) and Pindyck (1993) discuss two models that take time to build where the firms can invest at some maximum rate and abandon the projects in the mid stream. Thijssen (2015) proposed a model that can be used to value especially large-scale infrastructure projects, where the revenue process and construction process are possibly correlated. The concept of investment lag has also been used in the models of this thesis, which proves to have tremendous impacts on the project value and investment decisions.

Last, Trigeorgis (1993b) discussed the valuation of a project if multiple options exist in the same project. The sum of each option individually could be different from the combined option value, which is dependent on the option type, the degree of overlap of exercise regions and the sequence of options, etc. Thus valuing each option individually then summing the values will lead to the unreliable evaluation of the project. In chapter 5, a project with interactive options is presented and we show that the combined value of the options will further decrease if the project is run by two parties instead of one decision maker. The reason of a smaller combined value is due to the different goals of the two parties and that the exercise of one option limits the optimal exercise of the other. Thus the maximization problems that the two players solve are constrained.

[1] Investment lag was used by Bar-Ilan and Strange (1996), delivery lag was used by Alvarez and Keppo (2002) and implementation lag was used by Sarkar and Zhang (2013). These terms can be used interchangeably.

2.2 Health Technology Assessment Literature

After showing the various types of real options models that are related to the thesis, we next discuss the evaluation methods that are used by the majority in the pharmaceutical industry and the reasons why real options theory is better suited for evaluation of pharmaceutical R&D projects. In one word, the following evaluation methods that will be introduced are static analysis while real options approach is dynamic analysis.

Hartmann and Hassan (2006) present an in-depth analysis of collected empirical data regarding the application of different valuation methods in the pharmaceutical industry. Every pharmaceutical project can be considered as a series of sub-projects and is composed of several nodes including discovery, pre-clinical, phase I, II and III and approval. In each of these nodes, NPV/ENPV/DCF[2] are the most widely used methods for evaluation. The number of project managers who admit the adoption of these methods in each phases ranging from 59% to 100%. Others methods such as RoE/RoI/EVA[3], IRR (Internal Rate of Return), scoring model and real options analysis are also mentioned. But they are not as popular as NPV/ENPV/DCF.

Pandey (2003) discusses the pros and cons of evaluating a pharmaceutical R&D project by using NPV and ENPV (a probability-adjusted version of DCF is ENPV). It is argued that NPV is inferior since it assumes that decision makers are unable to take further actions such as abandonments based on future information while ENPV combines NPV and decision tree analyses by taking the probability distribution of future outcome into consideration. Indeed, decision tree helps decision makers by calculating the expected payoffs at every decision node so that better actions will be taken.

However, in real options point of view, even if the abandonment option is given, it does not necessarily need to be taken immediately. It is better to abandon the project when the information is bad enough or there is little chance that the project

[2]The most widely used evaluation methods in the pharmaceutical industry: NPV (Net Present Value), ENPV (Expected Net Present Value) and DCF (Discounted Cash Flow)

[3]Other evaluation methods in the pharmaceutical industry: ROE (Return on Equity), ROI (Return on investment) and EVA (Economic Value Added)

will be feasible anymore. At every decision node, ENPV computes the expected payoff of the project, however, the option value is not taken into account. Thus the project value is still underestimated. Neglecting the option values in the evaluation of project will lead to false rejection of the investment proposal.

Moreover, decision tree analysis is based on discrete time models and it is difficult for these models to capture the changes of NPV and option values for any given time compared to continuous time models. In addition, discrete time models can probably deal with problems on a case basis, but the lack of general results makes it more difficult to do comparative statics in general cases. These problems can be improved by using continuous time real options model.

ROE measures the profitability of a company by showing how much profits it generates with the money that shareholders have invested. ROI is computed as the difference of gain and cost from investment divided by cost of investment. It measures the efficacy of an investment and represents in a percentage term. EVA measures the value created that exceeds the required return from the company's shareholders and is computed as the net profit minus the opportunity cost of the capital of a firm.

Although these financial indicators provides useful information for comparisons between projects, they are static and not reliable for projects that have high volatility. For instance, the ROE is low if a firm decides to sacrifice a large part of the present earnings in change of a future earnings (Lesáková (2007)). But it does not necessarily indicate that the profitability of the firm is low. Moreover, these ratios fail to capture risks which lead to uncertainties. As a result, it is never recommended to treat these ratios as the only knowledge required to make investment decisions. They will have to be used in combination of other evaluation tools for better decision making.

IRR can be used to rank the multiple promising projects that a firm may want to invest. Generally speaking, the higher the IRR, the more profitable the project. However, in evaluation of the a pharmaceutical R&D project, the most difficult problem is to estimate the cash flows accurately because of uncertainties. IRR, which relies on the accurate approximation of cash flows, is a good measure on ranking

projects if the cash flows are certain. Thus, similar to other financial indicators, it is better used with combination of other evaluation methods that are able to estimate the expected cash flows.

Henriksen and Traynor (1999) proposed a flexible R&D project-selection method to rank R&D project alternatives, which relies on researcher-accepted peer review in the form of a user-friendly questionnaire. It was designed to help the federal research laboratory with funding selection. Although scoring models can be useful for valuing projects with relative values, they are not able to measure project values in absolute terms and thus comparative statics can hardly be applied. Moreover, they fail to capture the dynamics of the whole project. For instance, it is difficult for scoring models to explain how the project value changes in certain states and what leads to these changes.

Finally, real options theory is recommended to evaluate pharmaceutical R&D projects since most of these projects have the following properties: irreversibility of investment costs, managerial flexibility and uncertainty in cash flows. Irreversibility creates opportunity cost and value of waiting. Volatility of the project's payoffs makes managerial flexibility even more valuable. None of the above evaluation methods mentioned capture these properties, which lead to unreliable evaluation of project values.

It is not new to evaluate a pharmaceutical R&D project by using real options theory. For instance, Schwartz and Moon (1996) discusses the evaluation of a pharmaceutical R&D project when both cost and the completed value of the project are uncertain. Hsu and Schwartz (2008) studies the problem of under-investment in R&D for vaccines in the developing countries and the design of research incentives. In the thesis, we use continuous time real options models to solve the evaluation problems of the pharmaceutical R&D projects and provide with policy advices in terms of how to incentivize earlier investments and improve the quality of products.

2.3 Industrial Organization and Contract Theory Literature

The thesis is also related to the IO literature in that, in chapter 5, it analyzes how different structural arrangements of an R&D project will lead to different optimal investment threshold and optimal quality standard of the projects. The decentralized R&D project, which is run together by the government and a pharmaceutical company, and the social planner's project or the centralized project, are compared. This is similar to the vertical control problem in the relationship of an "upstream firm" and a "downstream firm" (Tirole (1988)).

However, there are some differences between the two frameworks. In this model, the relationship between the government and some pharmaceutical company is connected by an advance purchase commitments contract. The contract is proposed by the government, which ensures that the pharmaceutical company will receive some predetermined revenues once the requirements of the government are met. Thus the government moves first by setting the quality standard and the pharmaceutical company starts the R&D project next and keeps improving the quality of the product until the quality standard is reached.

The government is similar to the role of the downstream firm since the government first purchases the products from the pharmaceutical company and then sells them to the consumers. In the IO literature, however, the upstream firm usually moves first by selling the intermediate products to the downstream firms, and then to the retailers (downstream firm). After transformation of the intermediate products, the government sells the final products to consumers. Moreover, in terms of welfare analysis, this thesis' finding is similar to those in the IO literature, which shows that the value of the integrated firm is higher, but for a different reason.

For instance, Spengler (1950) argues that a vertical structure is more profitable under vertical integration than under a linear price since the monopoly profit of the vertical structure is realized. In addition, the social welfare is increased due to the elimination of the "double marginalization" problem. In this model, the

effects of the prices and demands of the intermediate and final product are not considered, the different projects' values are only dependent on the quality of the product. The reason for a higher value for the integrated project is because the maximization problems that the government and the pharmaceutical company solve are constrained, while the problem the social planner solves is unconstrained.

In addition, the relationship between the government and the pharmaceutical company can also be considered as a variation of the principal-agent relationship in the contract theory. The government can be viewed as the principal who maximizes the patients' welfare, while the pharmaceutical company is the agent, who maximizes profits and agrees to produce medicines for the government. For the government, it is better if the R&D project starts as soon as possible so that the quality of the drug will be reached sooner and the patients will have earlier access to the new products.

However, it is the pharmaceutical company who determines when to start the project. Because of uncertainty, starting the project as soon as possible is not always the best strategy (real options analysis). The decision maker will often choose to wait and invest when the conditions are favorable enough.

Although there is no asymmetric information in this model, the government is not able to control the pharmaceutical company's intention of earlier investment due to uncertainty. The only thing that can be observed is the exact investment timing because the different objectives of the two parties, the advance purchase commitments contract, does not lead to the first-best outcome in terms of social welfare.

This is similar to the moral hazard problem when the principal is not able to observe the effort of the agent but only the outcomes (Bolton and Dewatripont (2005)), though the outcomes are merely noisy signal of effort. Hence the principal will need to incentivize the agent to exert more effort by designing an effective managerial incentive schemes. Similarly, in our model, the government will also need to incentivize the pharmaceutical company to start the project earlier by altering the quality standard of the project or the remuneration level. More importantly, we

show that uncertainty, like asymmetric information, will also lead to a sub-optimal outcome in a two-parties contract.

Chapter 3

Basic Tools from Real Options Theory

3.1 Probability Spaces and Filtrations

In this chapter we review some basic concepts from probability theory and the basic tools from the real options theory that have been used in the thesis.

To start with, the probability spaces are first defined, in which the stochastic processes, expectations and probability measures that have been used in the thesis are dependent on.

Definition 3.1.1 *(Oksendal (2013)) If Ω is a given set, then a σ-algebra $\mathscr{F}$ on Ω is a family $\mathscr{F}$ of subsets of Ω with the following properties:*
(a) $\emptyset \in \mathscr{F}$
(b) $F \in \mathscr{F} \Longrightarrow F^c \in \mathscr{F}$, where F^c=$\Omega \backslash F$ is the complement of F in Ω
(c) $A_1, A_2 ... \in \mathscr{F} \Longrightarrow A := \bigcup_{i=1}^{\infty} A_i \in \mathscr{F}$
The pair $(\Omega, \mathscr{F})$ is called a measurable space. A probability measure P on a measurable space $(\Omega, \mathscr{F})$ is a function $P : \mathscr{F} \longrightarrow [0,1]$ such that
(a) $P(\emptyset) = 0, P(\Omega) = 1$
(b) if $A_1, A_2 ... \in \mathscr{F}$ and $\{A_i\}_{i=1}^{\infty}$ is disjoint (i.e. $A_i \cap A_j = \emptyset$ if $i \neq j$) then

$$P\left(\bigcup_{i=1}^{\infty} A_i\right) = \sum_{i=1}^{\infty} A_i. \tag{3.1}$$

The triple $(\Omega, \mathscr{F}, P)$ *is called a probability space.*

Definition 3.1.2 *Given a measurable space* $(\Omega, \mathscr{F})$*, a filtration is a sequence of* σ*-algebras* $\{\mathscr{F}_t\}_{t\geq 0}$ *with* $\mathscr{F}_t \subseteq \mathscr{F}$ *where each* t *is a non-negative real number and* $t_1 \leq t_2 \implies \mathscr{F}_{t_1} \subseteq \mathscr{F}_{t_2}$.

The filtration at time t represents all the historical information available at time t.

3.2 Brownian Motion

The Brownian Motion is often used to develop models for a decision making process in which action is taken when a threshold criterion level is reached. Moreover, Brownian Motion acts as random part of the stochastic processes such as Arithmetic Brownian Motion (ABM) and Geometric Brownian Motion (GBM), which are widely used to model different uncertainties in the investment problems.

Definition 3.2.1 *(Billingsley (1995)) A Brownian motion or Wiener process is a stochastic process* $[W_t : t \geq 0]$*, on some* $(\Omega, \mathscr{F}, P)$*, with the three properties:*
(a) The process starts at 0: $P[W_0 = 0] = 1$.
(b) The increments are independent: If $0 \leq t_0 \leq t_1 \leq ... \leq t_k$*, then*

$$P[W_{t_i} - W_{t_{i-1}} \in H_i, i \leq k] = \prod_{i\leq k} P[W_{t_i} - W_{t_{i-1}} \in H_i]. \tag{3.2}$$

(c) For $0 \leq s < t$ *the increment* $W_t - W_s$ *is normally distributed with mean* 0 *and variance* $t - s$*:*

$$P[W_t - W_s \in H] = \frac{1}{\sqrt{2\pi(t-s)}} \int_H e^{-x^2/2(t-s)} dx. \tag{3.3}$$

Note that the notation W_t is often interchangeable with B_t.

3.3 Ito Diffusions, Ito's Lemma and Geometric Brownian Motion (GBM)

Definition 3.3.1 *(Thijssen (2013b)) The stochastic process $(Y_t)_{t\geq 0}$, where for each $t > 0$, is*

$$Y_t = y + \int_0^t \mu(s, Y_s)ds + \int_0^t \sigma(s, Y_s)dB_s, \quad Y_0 = y, \quad P_s - a.s., \tag{3.4}$$

and $(B_t)_{t\geq 0}$ is a Brownian motion. Processes as in Equation 3.4 are called (Ito) diffusions.

In differential notation we can write

$$dY_t = \mu(t, Y_t)dt + \sigma(t, Y)dB_t. \tag{3.5}$$

An equation of the form (Equation 3.5) is also called a stochastic differential equation (SDE), the function $\mu(\cdot)$ is the trend and $\sigma(\cdot)$ is the volatility. If the trend and volatility do not depend on t, the diffusion is time homogeneous.

Ito's Lemma is of great importance in the Ito Calculus and it can be used to compute the derivative of a time-dependent function of a stochastic process. It plays the role of the chain rule in a stochastic setting, similar to the chain rule in ordinary differential calculus. In the thesis, we model the uncertainty in the investment problems by using stochastic processes that the NPV functions and the functions of project values are dependent on. Ito's Lemma can be used to calculate the change of NPV or project values within an infinite small amount of time for any given time. This is crucial in real options analysis since decision makers will need to compare

the NPV and option value of waiting as time goes by, so that an optimal investment decision can be made.

Definition 3.3.2 *(Thijssen (2013b)) Ito's Lemma. Let $(Y_t)_{t\geq 0}$ follow an Ito diffusion and let $X_t = g(t,Y_t)$, with g being a twice continuously differentiable function. Then*

$$\begin{aligned} dX_t =& \frac{\partial g(\cdot)}{\partial t}dt + \frac{\partial g(\cdot)}{\partial Y_t}dY_t + \frac{1}{2}\frac{\partial^2 g(\cdot)}{\partial Y_t^2}dY_t^2 \\ =& \left[\frac{\partial g(\cdot)}{\partial t} + \frac{\partial g(\cdot)}{\partial Y_t}\mu(\cdot) + \frac{1}{2}\frac{\partial^2 g(\cdot)}{\partial Y_t^2}\sigma(\cdot)^2\right]dt + \frac{\partial g(\cdot)}{\partial Y_t}\sigma(\cdot)dB_t. \end{aligned} \tag{3.6}$$

Geometric Brownian Motion is used in the thesis to model the uncertainties in such as revenues and quality of drugs, which are assumed to be non-negative.

Definition 3.3.3 *A Geometric Brownian Motion (GBM) Y_t is the solution of an SDE with linear drift and diffusion coefficients, i.e.*

$$dY_t = \mu Y_t dt + \sigma Y_t dB_t, \tag{3.7}$$

with initial value $Y_0 = y$.

3.4 Stopping Time

Definition 3.4.1 *(Oksendal (2013)) Let $\mathcal{N}_t$ be an increasing family of σ-algebras (of subsets of Ω). A function $\Omega \to [0,\infty]$ is called a (strict) stopping time w.r.t. $\mathcal{N}_t$ if*

$$\{\omega; \tau(\omega) \leq t\} \in \mathcal{N}_t, for\ all\ t \geq 0. \tag{3.8}$$

In other words, it should be possible to decide whether or not $\tau \leq t$ has occurred on the basis of the knowledge of $\mathcal{N}_t$.

For instance, if a firm decides to invest as soon as some pre-determined threshold (or "trigger") Y^* is reached, then the (random) time at which investment takes place

is the first hitting time

$$\tau(Y^*) = \inf\{t \geq 0 \mid Y_t \geq Y^*, Y_0 = y\}, \tag{3.9}$$

which is a stopping time.

3.5 The Generator of a Diffusion and Dynkin's Formula

Definition 3.5.1 *(Oksendal (2013)) Let Y_t be a (time-homogeneous) Ito diffusion in R^n. The (infinitesimal) generator A of Y_t is defined by*

$$Af(y) = \lim_{t \to 0} \frac{E^y[f(Y_t)] - f(y)}{t}; \quad y \in R^n \tag{3.10}$$

The set of functions $f : R^n \to R$ such that the limit exists at y is denoted by $\mathscr{D}_A(y)$, while $\mathscr{D}_A$ denotes the set of functions for which the limit exists for all $y \in R^n$.

Another operator which is closely related to the generator A, but is more suitable in many situations, is the *characteristic operator* of the diffusion process $(Y_t)_{t \geq 0}$. In the thesis, Y_t follows GBM, if there exists a function $f \subset \mathscr{C}^2$, the generator A is equal to the characteristic operator which is denoted by $\mathscr{L}$. Expand the characteristic operator by using Ito's Lemma, we have

$$A_Y = \mathscr{L}_Y = \frac{1}{2}\sigma^2 y^2 \frac{\partial^2}{\partial y^2} + \mu y \frac{\partial}{\partial y}. \tag{3.11}$$

The characteristic operator of a diffusion process can be used to compute the value of waiting within an infinite small amount of time in the real options analysis.

Definition 3.5.2 *(Oksendal (2013)) Dynkin's formula. Let $f \in \mathscr{C}_0^2(R^n)$. Suppose τ is a stopping time, $E^y[\tau] < \infty$. Then*

$$E^y[f(Y_\tau)] = f(y) + E^y\left[\int_o^\tau Af(Y_s)ds\right]. \tag{3.12}$$

Dynkin's formula is used in the thesis to calculate the expected discount factor at the optimal investment timing, when the underlying stochastic process $(Y_t)_{t\geq 0}$ follows GBM.

(Thijssen (2013b))In the models, we will often need to compute $E_y[e^{-\rho\tau}F(Y_\tau)]$, for some stopping time τ and a discount rate ρ, where F is an increasing and concave $\mathscr{C}^2$ function.

Define the process $(X_t)_{t\geq 0}$ by

$$X_t = \begin{bmatrix} s+t \\ Y_t \end{bmatrix}$$

and for any function $g \in \mathscr{C}^2([0,\infty)\times E)$, the generator of g equals

$$\mathscr{L}_X g = \frac{\partial g}{\partial t} + \frac{1}{2}\sigma^2 y^2 \frac{\partial^2 g}{\partial y^2} + \mu y \frac{\partial g}{\partial y}. \tag{3.13}$$

It follows that for $g(t,y) = e^{-\rho t}F(y)$ we get:

$$\begin{aligned} \mathscr{L}_X g =& e^{-\rho t}\left(\frac{1}{2}\sigma^2 y^2 \frac{\partial^2 F}{\partial y^2} + \mu y \frac{\partial F}{\partial y} - \rho F\right) \\ =& e^{-\rho t}\left(\mathscr{L}_Y F - \rho F\right). \end{aligned} \tag{3.14}$$

Dynkin's formula then gives

$$E_y\left[e^{-\rho\tau}F(Y_\tau)\right] = F(y) + E_y\left[\int_0^\tau e^{-\rho t}\left(\mathscr{L}_Y F(Y_t) - \rho F(Y_t)\right)dt\right]. \tag{3.15}$$

If $\mathscr{L}_Y F(Y_t) - \rho F(Y_t) = 0$ holds and $\varphi(\cdot)$ is known to be the general solution, the expected discounted factor can be computed as

$$E_y\left[e^{-\rho\tau}\right] = \frac{\varphi(y)}{\varphi(Y_\tau)}. \tag{3.16}$$

It is worth noting that the above equation is not specific to Geometric Brownian Motion (GBM), it is a generalized result which can be applied to any stochastic processes. However, for other stochastic processes that are not GBM, one cannot guarantee that $\varphi(\cdot)$, which solves the PDE in equation (3.13), has a closed form solution. Thus the expected discount factor may not be computed. For GBM, the functional form of the solution to equation (3.13) is known, which enables us to further calculate the expected discount factor.

3.6 Markov Property and Strong Markov Property

Definition 3.6.1 *(Oksendal (2013)) Markov property. Let f be a bounded Borel function from R^n to R. Then, for $t, h \geq 0$*

$$E^x\left[f(X_{t+h}) \mid \mathscr{F}_t^{(m)}\right]_{(\omega)} = E^{X_t(\omega)}\left[f(X_h)\right]. \tag{3.17}$$

Definition 3.6.2 *(Oksendal (2013)) Strong Markov property. Let f be a bounded Borel function on R^n, τ a stopping time w.r.t. $F_t^{(m)}$, $\tau < \infty$ a.s. Then*

$$E^x\left[f(X_{\tau+h}) \mid \mathscr{F}_\tau^{(m)}\right] = E^{X_\tau}\left[f(X_h)\right] \quad \textit{for all} \quad h \geq 0. \tag{3.18}$$

The uncertainties of the investment problems in the thesis are modeled by GBM. Moreover, GBM is Markovian which satisfies the above two properties which makes the computation much easier. For instance, if the decision maker, at time $s > 0$, wants to compute the expected project value at time $t > s$, because of the Markovian

property of GBM, the decision maker may treat time t as the new start and compute the project value at time t then discount it back to time s.

3.7 Law of Iterated Expectation

Definition 3.7.1 *(Billingsley (1995)) If X is integrable and the σ-fields $\mathscr{G}_1$ and $\mathscr{G}_2$ satisfy $\mathscr{G}_1 \subset \mathscr{G}_2$, then*

$$E[E[X \mid \mathscr{G}_2] \mid \mathscr{G}_1] = E[X \mid \mathscr{G}_1] \tag{3.19}$$

3.8 Poisson Process

Let $(T_0, T_1, ...)$ be a strictly increasing sequence of stopping times, in a sense that for any $i, j \in N$ with $i < j$, $T_i < T_j$ a.s., with $T_0 = 0$. Define the indicator function

$$1_{\{t \geq T_n\}} = \begin{cases} 1 & if \quad t \geq T_n(\omega) \\ 0 & if \quad t < T_n(\omega). \end{cases} \tag{3.20}$$

Definition 3.8.1 *(Thijssen (2013b)) The counting process associated with the sequence $(T_0, T_1, ...)$ is the process $(N_t)_{t \geq 0}$ defined by $N_t = \sum_{n \geq 0} 1_{\{t \geq T_n\}}$. Note that $(N_t)_{t \geq 0}$ takes values in $\{0, 1, 2, ...\}$. Let $T := \sup T_n$. We say that $(N_t)_{t \geq 0}$ is a counting process without explosions if $T = \infty$, P-a.s.*

Definition 3.8.2 *A counting process without explosions is a Poisson process if*
(1) $N_t - N_s$ is independent of N_s, for all $s < t$;
(2) for any $s < t$ and $u < v$, with $t - s = v - u$ it holds that $N_t - N_s$ and $N_v - N_u$ have the same distribution.

The Poisson process is used to model the sudden success of the pharmaceutical R&D project in chapter 6.

Chapter 4

The Effect of Commercialization Flexibility and Investment Lag on Pharmaceutical Investment Decisions under Uncertainty

4.1 Abstract

This chapter studies the evaluation of irreversible pharmaceutical R&D projects and optimal exercise of the options to defer investment and commercialization in the presence of stochastic payoffs and investment lag. Two pharmaceutical R&D projects, with and without commercialization flexibility, are analyzed and compared. The project with commercialization flexibility is modeled as a compound option, which is composed of an option to defer starting the R&D process and an option to defer commercialization, with the investment lag in the R&D process. Thus the revenues are not necessarily generated after construction being finished, which is usually assumed in the literature. We find that, although a project with commercialization flexibility has a higher project value, it does not provide with

more investment incentives when uncertainty is high. In addition, the fast approval policy is more effective in terms of shortening the time for new drugs to be on the market only when uncertainty is low.

4.2 Introduction

The development of modern medical science has helped to cure many diseases that were once considered as "the incurables" such as Smallpox and the Black Death. However, when facing diseases such as cancer, AIDS and Avian flu, which have been claiming thousands of lives, we still strive to develop new technologies and look for better solutions. One of the approaches that have been discussed widely in the literature on how to satisfy the clinical needs for these patients earlier is by shortening the approval process.

In 1992, the US Food and Drug Administration (FDA) initiated the FDA Accelerated Approval Program to allow faster approval of drugs for serious conditions that fill an unmet medical need.[1] In April 2014, the Medicines and Healthcare products Regulatory Agency (MHRA) in the UK launched the Early Access to Medicines Scheme (EAMS) in order to give patients with life threatening or seriously debilitating conditions access to medicines that do not yet have a marketing authorization and where there are no suitable alternative licensed treatments.[2]

However, from the perspective of a pharmaceutical company who provides profitability, is it an optimal strategy to launch and start selling the new drug as soon as the products are approved? By looking at the top 10 blockbuster drugs launched in US from 2010-2013, it is found that half of the pharmaceutical companies (8/18) chose to launch the new drugs as soon as their products were approved[3], while the other half of the companies (7/18) delayed the launch, including Lipitor and Plavix,

[1] http://www.fda.gov/Drugs/ResourcesForYou/HealthProfessionals/ucm313768.htm

[2] http://www.mhra.gov.uk/Howweregulate/Innovation/EarlyaccesstomedicinesschemeEAMS/index.htm

[3] The time between approval and launch is less than a month. The approval dates are collected from FDA's website http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm and the start dates of drugs are collected by the annual reports of each pharmaceutical companies that produced them. Among all the drugs, the launch dates of 3/18 drugs cannot be found

of which sales ranked 1 and 2 in 2010. In this chapter, we explain the behaviors of the companies by using real options theory to model a pharmaceutical investment and commercialized decision.

Following Myers (1977), it is quite natural to think of many investment problems that feature irreversibility, flexibility and uncertainty as real options. Many R&D projects can be fitted in this framework since they exhibit these features. First, the cost spent on developing a drug is usually high and irreversible since it will not be recovered if the research turns out to be a failure or the project is abandoned. Second, most of the decisions do not have to be made abruptly. Waiting to decide while collecting useful information will be a better choice. Last, the payoffs of projects are usually full of uncertainties in that the price and demand of drugs are usually not known ex ante. Because of these features, initiating the project at different time will lead to huge differences on the potential profits.

The evaluation of a pharmaceutical R&D project by using real options theory is not new in the literature. For instance, Schwartz and Moon (1996) discuss the evaluation of a pharmaceutical R&D project when both cost and the completed value of the project are uncertain. Hsu and Schwartz (2008) studies the problem of under-investment in R&D for vaccines in the developing countries and the design of research incentives.

An additional feature for many pharmaceutical R&D projects is that it often takes a long time, 8-14 years average, to complete the R&D process before approval and commercialization (DiMasi et al. 2003). In real options literature, the duration of time between the start and completion of a project is called the investment lag, delivery lag or implementation lag [4], which has been used to model construction delays in many papers. Alvarez and Keppo (2002) consider a model of investment where investment lag is dependent on the underlying stochastic process. They find that the impact of delivery lag on investment is negative. In other words, an increase in the investment lag delays investment. Sarkar and Zhang (2013) argue

[4]Investment lag was used by Bar-Ilan and Strange (1996), delivery lag was used by Alvarez and Keppo (2002) and implementation lag was used by Sarkar and Zhang (2013). These terms can be used interchangeably.

that the conventional result "increase in uncertainty and investment lag should have inhibiting effect on investment" can be reversed if the project has sufficient reversibility. Majd and Pindyck (1987) and Pindyck (1993) discuss two models that take time to build where the firms can invest at some maximum rate and abandon the projects in the mid stream. The difference is the former paper introduce uncertainty in the value of the completed project where the latter in the cost. Thijssen (2015) proposed a model that can be used to value especially large-scale infrastructure projects, where the revenue process and construction process are possibly correlated.

However, the decisions in the papers mentioned above are either "once-and-for-all" type decisions (see Alvarez and Keppo (2002)) or composed of the abandonment options in the mid stream or at the completion of the projects. Moreover, these papers assume that the revenues or the salvage value will be generated at the completion of the project (see Sarkar and Zhang 2013).

In this chapter, we model an R&D project with investment lag and commercialization flexibility. Thus the revenues are not necessarily generated as soon as the R&D process is completed. The payoffs of the project are modeled by a stochastic process $(Y_t)_{t\geq 0}$ that follows Geometric Brownian Motion (GBM). Dependent on the value of the stochastic process at the end of the R&D process, the decision maker will consider whether to start commercialization immediately or delay it. If commercialization is delayed, the revenues will also be generated later.

Since starting the R&D process is a prerequisite of acquiring the option to launch the products afterwards, the decision maker's problem can be considered as a compound option. Methodologically, the major contribution of this chapter is to model an R&D project by combining a compound option with investment lag. The combination of the two problems further increases the difficulty of making an optimal investment decision under uncertainty since the expected NPV of the project are influenced in both directions. First, the investment lag will increase the discounting on future payoffs, which reduces the NPV of the project. A lower NPV will lead to a higher investment threshold. Second, the investment lag will have effects on the probability that the commercialization process will take place,

which may increase the NPV of the project and lead to a lower investment threshold. Last, an increase in the investment lag will increase the option value of waiting if the volatility of the stochastic process $(Y_t)_{t\geq 0}$ is high which will lead to a high investment threshold. Hence the effect of investment lag on option value is not clear. The interactions of these effects make the evaluation of a project more difficult.

There are three major findings of this chapter. First, the project with commercialization flexibility performs better when uncertainty is low since both the probabilities of investment and commercialization taking place are higher. Second, the project without commercialization flexibility is better in terms of sooner investment and commercialization when uncertainty is high. Last, fast approval, which is modeled by shortening the investment lag, is a better policy when uncertainty is low.

The remainder of the chapter is organized as follows. Section 4.3 introduces the model without commercialization flexibility. Section 4.4 discusses the model with commercialization flexibility. In section 4.5, the two projects are compared. Section 4.6 considers policy implications. Finally, section 4.7 concludes the chapter.

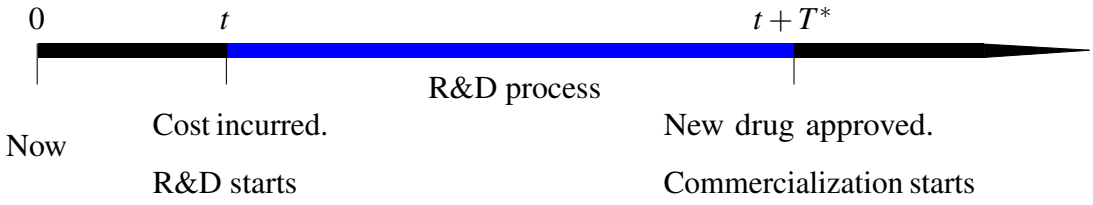
4.3 The Project with Immediate Commercialization

It is worth noting that the following model and results are not new in the real options literature. They serve as benchmarks in order to compare with the model and results in section 4.4. The model can be considered as a simplified version of the model of Alvarez and Keppo (2002), when the sunk cost is paid when the investment takes place and when the investment lag is a known constant instead of a function dependent on the underlying stochastic process.

Consider a pharmaceutical company that is provided with the opportunity to invest in a drug development project with uncertain revenues. The first, R&D, phase of the project, starts when the cost flow C_R commences. The second, commercialization, phase of the project, starts when the new drug is approved, which we assume happens after a known, fixed time T^*. As soon as the drug is approved and ready to

launch, the company will start selling it immediately by paying a sunk cost $I_c > 0$ with revenues being generated at this point.

The time line of the project is as follows



Uncertainty in revenues is represented by a stochastic process $(Y_t)_{t\geq 0}$, which follows a geometric Brownian motion

$$dY_t = \mu Y_t dt + \sigma Y_t dB_t, \tag{4.1}$$

where $(B_t)_{t\geq 0}$ is a Wiener process. We assume that the initial value is known with $Y_0 = y$. The probability measure over the sample paths of $(Y_t)_{t\geq 0}$ is denoted by P_y.

It is assumed that the decision maker is risk neutral and $\rho > 0$ is the discount rate. When the new drug is available to sell at the end of the R&D process, the decision maker will start the commercialization process immediately by paying a sunk cost I_c in return for a stream of revenues. The expected profit of commercialization is

$$\begin{aligned} F_c(y) &= E_y\left(\int_0^\infty e^{-\rho t} Y_t dt\right) - I_c \\ &= \frac{y}{\rho - \mu} - I_c, \end{aligned} \tag{4.2}$$

where E_y is the expectation operator under the probability measure P_y. In addition, we assume that $\rho > \mu$, to ensure finiteness of $F_c(y)$. To simplify the problem, we also assume the operating cost of commercialization process is 0. However, the following results will not lose generality if operating cost is added since it can be considered as part of the sunk cost.

At time 0, the problem of the decision maker is to find the optimal stopping time τ_1 to start the project. Since $F_c(Y_{t+T^*})$ is a random variable at time t, the

problem faced by the decision maker is to optimally stop the expected profit of commercialization $E_{Y_t}[F_c(Y_{t+T^*})]$, net of R&D costs. That is, the decision maker needs to solve the optimal stopping problem

$$\begin{aligned} G(y) &= \sup_{\tau_1} E_y \left[-\int_{\tau_1}^{\tau_1+T^*} e^{-\rho t} C_R dt + e^{-\rho(\tau_1+T^*)} \left(\frac{Y_{\tau_1+T^*}}{\rho-\mu} - I_c \right) \right] \\ &= \sup_{\tau_1} E_y \left\{ e^{-\rho\tau_1} \left[e^{-\rho T^*} E_{Y_{\tau_1}} \left[\frac{Y_{\tau_1+T^*}}{\rho-\mu} - I_c \right] - \frac{c_R(1-e^{-\rho T^*})}{\rho} \right] \right\} \\ &\equiv \sup_{\tau_1} E_y \left[e^{-\rho\tau_1} g(Y_{\tau_1}) \right], \end{aligned} \tag{4.3}$$

where

$$g(y) = \frac{y e^{-(\rho-\mu)T^*}}{\rho-\mu} - I_c e^{-\rho T^*} - \frac{c_R(1-e^{-\rho T^*})}{\rho}. \tag{4.4}$$

As is well-known, for this type of problem, the optimal stopping time takes the form of the first hitting time of some threshold Y^*, i.e., $\tau(Y^*) = \inf\{t \geq 0 \mid Y_t \geq Y^*, Y_0 = y\}$. (Basically, because of the Markovian nature of the process and monotonicity of g in y.) In addition, the space $[0,\infty]$ can be divided into two regions by the critical value Y^*. In $[0,Y^*)$, continuation (waiting) is optimal since the value of investing immediately is less than the value of waiting. In $[Y^*,\infty]$, termination (invest immediately) is optimal since the value of investing immediately exceeds the value of waiting. Hence $[0,Y^*)$ is called the continuation region while $[Y^*,\infty]$ is called the stopping region (Dixit and Pindyck (1994)). Thus, instead of solving the optimal stopping problem in equation 4.3, we can compute the optimal investment threshold Y^* by rewriting the problem above as

$$\begin{aligned} G(y) &= \sup_{Y^*} E_y \left[e^{-\rho\tau_1(Y^*)} g(Y_{\tau_1(Y^*)}) \right] \\ &= \sup_{Y^*} E_y \left[e^{-\rho\tau_1(Y^*)} \right] g(Y^*). \end{aligned} \tag{4.5}$$

The characteristic operator of the process $(Y_t)_{t\geq 0}$ is

$$\mathscr{L}_Y = \frac{1}{2}\sigma^2 y^2 \frac{\partial^2}{\partial y^2} + \mu y \frac{\partial}{\partial y}. \tag{4.6}$$

Since the Bellman equation holds in the continuation region, i.e., $\mathscr{L}_Y G = \rho G$. By substituting the expression of the characteristic operator and rearranging, we have

$$\frac{1}{2}\sigma^2 y^2 \frac{\partial^2 G}{\partial y^2} + \mu y \frac{\partial G}{\partial y} - \rho G = 0, \tag{4.7}$$

of which the general solution is of the form

$$G(y) = Ay^{\beta_1} + By^{\beta_2}, \tag{4.8}$$

where $\beta_1 > 1$ and $\beta_2 < 0$ are the two roots of the quadratic equation

$$\mathscr{Q}(\beta) = \frac{1}{2}\sigma^2 \beta(\beta-1) + \mu\beta - \rho = 0. \tag{4.9}$$

The boundary condition $G(0) = 0$ is satisfied only if $B = 0$. Thus the general solution of the value function is reduced to be $G(y) = Ay^{\beta_1}$ on $(0, Y^*)$.

By using Dynkin's formula (Oksendal (2013)), the expected discount factor is

$$E_y\left[e^{-\rho\tau(Y^*)}\right] = \frac{G(y)}{G(Y^*)} = \left(\frac{y}{Y^*}\right)^{\beta_1}. \tag{4.10}$$

The optimal investment threshold Y^* can be obtained by substituting the expected discount factor $E_y\left[e^{-\rho\tau(Y^*)}\right]$ in equation 4.10 with the result in Equation 4.5 and taking the first order derivatives of the value function $G(y)$ with respect to Y^*

$$G(Y^*)g'(Y^*) = G'(Y^*)g(Y^*), \tag{4.11}$$

and

$$Y^* = \frac{\beta_1}{\beta_1 - 1}(\rho - \mu)e^{(\rho-\mu)T^*}\left(I_c e^{-\rho T^*} + \frac{c_R(1 - e^{-\rho T^*})}{\rho}\right). \tag{4.12}$$

In particular, if there is no investment lag, i.e., $T^* = 0$,

$$Y^* = \frac{\beta_1}{\beta_1 - 1}(\rho - \mu)I_c, \tag{4.13}$$

which is the standard investment threshold in Dixit and Pindyck (1994).

Dependent on the current value of y, the value of the project is

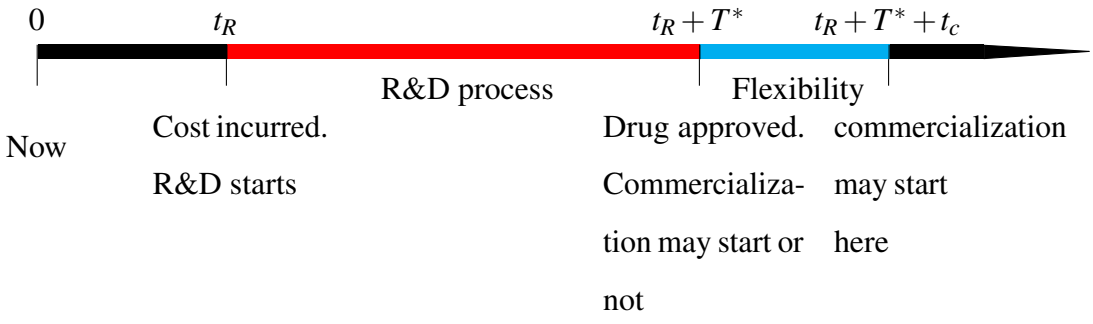
$$G(y) = \begin{cases} \left(\frac{y}{Y^*}\right)^{\beta_1}\left(\frac{Y^* e^{-(\rho-\mu)T^*}}{\rho-\mu} - I_c e^{-\rho T^*} - \frac{c_R(1-e^{-\rho T^*})}{\rho}\right) & if \quad y < Y^* \\ \frac{y e^{-(\rho-\mu)T^*}}{\rho-\mu} - I_c e^{-\rho T^*} - \frac{c_R(1-e^{-\rho T^*})}{\rho} & if \quad y \geq Y^*. \end{cases} \tag{4.14}$$

The value of the project with immediately commercialization at any point in time is dependent on the value of the stochastic process $(Y_t)_{t\geq 0}$, which represents the revenue of the product at that time. If the project's revenue is less than the optimal investment threshold Y^*, the best strategy is to wait and only pay the sunk cost as soon as Y^* is reached. If the project's revenue is greater or equal to the optimal investment threshold Y^*, the best strategy is to invest and start the R&D process immediately.

4.4 The Project with Commercialization Flexibility

In section 4.3, we discussed a project assuming that the pharmaceutical company starts commercialization immediately after the R&D process finishes. Now, we relax this assumption by providing commercialization flexibility at the approval date so that the decision maker is allowed to delay commercialization. In this case, two decisions will need to be made by the decision maker, which are the optimal time (i) to start the project and (ii) to commence commercialization.

By offering the commercialization flexibility, the time line of the project is as follows:



The problem of the decision maker now is to maximize the expected discounted net present value of the project when she has both the option to defer the decision of investment and the option to defer commercialization. The problem can be solved by backwards induction.

Suppose that the R&D process is finished and that the new drug is ready for commercialization, the expected revenues net of associated sunk costs of the commercialization process is

$$F_c(y) := E_y\left(\int_0^\infty e^{-\rho t} Y_t dt - I_c\right) = \frac{y}{\rho - \mu} - I_c. \tag{4.15}$$

The value of the commercialization process is determined by the solution to the associated optimal stopping problem. As in the previous section, the optimal policy is of the threshold type, so that we can write

$$\begin{aligned} F_c^*(y) &:= \sup_\tau E_y\left[e^{-\rho\tau} F(Y_\tau)\right] \\ &= \sup_{Y_c^*} E_y\left[e^{-\rho\tau(Y_c^*)} F(Y_{\tau(Y_c^*)})\right] \\ &= \sup_{Y_c^*} E_y\left[e^{-\rho\tau(Y_c^*)}\right] F(Y_c^*). \end{aligned} \tag{4.16}$$

Following the same approach as in section 4.3, we are able to compute the threshold for commercialization as

$$Y_c^* = \frac{\beta_1}{\beta_1 - 1}(\rho - \mu)I_c. \tag{4.17}$$

The value function of the commercialization option is

$$F_c^*(y) = \begin{cases} \left(\frac{y}{Y_c^*}\right)^{\beta_1}\left(\frac{Y_c^*}{\rho-\mu} - I_c\right) & if \quad y < Y_c^* \\ \frac{y}{\rho-\mu} - I_c & if \quad y \geq Y_c^*. \end{cases} \tag{4.18}$$

In what follows, the two terms $\left(\frac{y}{Y_c^*}\right)^{\beta_1}\left(\frac{Y_c^*}{\rho-\mu} - I_c\right)$ and $\frac{y}{\rho-\mu} - I_c$ in the value function above will be used frequently. For simplicity, define $C(y;Y_c^*) = \left(\frac{y}{Y_c^*}\right)^{\beta_1}\left(\frac{Y_c^*}{\rho-\mu} - I_c\right)$ and $D(y) = \frac{y}{\rho-\mu} - I_c$. If R&D starts at time t, then, Y_{t+T^*} is a random variable that is not $\mathscr{F}_t$ measurable. In other words, the exact values of $C(Y_{t+T^*};Y_c^*)$, $D(Y_{t+T^*})$ and $F_c^*(Y_{t+T^*})$ are unknown with the information up to time t. So, to evaluate the option to invest in R&D, the decision maker must rely on the conditional expectations $E_{Y_t}\left(C(Y_{t+T^*};Y_c^*)|Y_{t+T^*} < Y_c^*\right)$, $E_{Y_t}\left(D(Y_{t+T^*})|Y_{t+T^*} \geq Y_c^*\right)$ and $E_{Y_t}[F_c^*(Y_{t+T^*})]$, which are given by

Lemma 4.1

$$E_{Y_t}\left(C(Y_{t+T^*};Y_c^*)|Y_{t+T^*} < Y_c^*\right) = (Y_t)^{\beta_1} e^{[\mu\beta_1 + \frac{1}{2}\sigma^2\beta_1(\beta_1-1)]T^*}(Y_c^*)^{-\beta_1}\left(\frac{Y_c^*}{\rho-\mu} - I_c\right) \tag{4.19}$$

and

$$E_{Y_t}\left(D(Y_{t+T^*})|Y_{t+T^*} \geq Y_c^*\right) = \frac{Y_t e^{\mu T^*}}{\rho-\mu} - I_c. \tag{4.20}$$

Since $F_c^*(Y_{t+T^*})$ is a random variable at time t, by the law of total expectation, the expected value is

$$E_{Y_t}[F_c^*(Y_{t+T^*})] = [E_{Y_t}(C(Y_{t+T^*};Y_c^*)|Y_{t+T^*} < Y_c^*)]P_{Y_t}(Y_{t+T^*} < Y_c^*) + [E_{Y_t}(D(Y_{t+T^*})|Y_{t+T^*} \geq Y_c^*)]P_{Y_t}(Y_{t+T^*} \geq Y_c^*). \quad (4.21)$$

The two probabilities $P_{Y_t}(Y_{t+T^*} < Y_c^*)$ and $P_{Y_t}(Y_{t+T^*} \geq Y_c^*)$ in the above equations are

$$P_{Y_t}(Y_{t+T^*} < Y_c^*) = P_{Y_t}\left(\frac{\log(\frac{Y_{t+T^*}}{Y_t}) - (\mu - \frac{1}{2}\sigma^2)T^*}{\sigma\sqrt{T^*}} < \frac{\log(\frac{Y_c^*}{Y_t}) - (\mu - \frac{1}{2}\sigma^2)T^*}{\sigma\sqrt{T^*}}\right) \quad (4.22)$$

and

$$P_{Y_t}(Y_{t+T^*} \geq Y_c^*) = 1 - P_{Y_t}(Y_{t+T^*} < Y_c^*). \quad (4.23)$$

See proof of the lemma in the Appendix.

After computing the expected NPV of the commercialization process, the decision maker needs to find the optimal time to start the R&D process. The corresponding optimal stopping problem is

$$\begin{aligned} F_R^*(y) &= \sup_{\tau_1} E_y\left\{e^{-\rho\tau_1}\left[e^{-\rho T^*}E_{Y_{\tau_1}}[F_c^*(Y_{\tau_1+T^*})] - \frac{c_R(1-e^{-\rho T^*})}{\rho}\right]\right\} \\ &\equiv \sup_{\tau_1} E_y\left[e^{-\rho\tau_1}f_R(Y_{\tau_1})\right], \end{aligned} \quad (4.24)$$

where

$$f_R(Y_{\tau_1}) = e^{-\rho T^*}\Big[E_{Y_{\tau_1}}(C(Y_{\tau_1+T^*};Y_c^*|Y_{\tau_1+T^*}<Y_c^*)P_{Y_{\tau_1}}(Y_{\tau_1+T^*}<Y_c^*) + E_{Y_{\tau_1}}(D(Y_{\tau_1+T^*}|Y_{\tau_1+T^*}\geq Y_c^*)P_{Y_{\tau_1}}(Y_{\tau_1+T^*}\geq Y_c^*)\Big] - \frac{c_R(1-e^{-\rho T^*})}{\rho}. \tag{4.25}$$

The above problem is closely related to the one proposed by Alvarez and Keppo (2002). In their model, the investment lag T^* is assumed to be a function of the revenue process, and payoffs are received at the end of the lag. While the investment lag is an exogenously given constant in our problem and the project is considered as a compound option because of commercialization flexibility. To maximize the value of the project, both investment and commercialization decisions will need to be taken into account simultaneously.

Conjecture 4.1 *There exists a unique investment threshold $\hat{Y}$ that maximizes the value of the project with commercialization flexibility. This threshold $\hat{Y}$ satisfies*

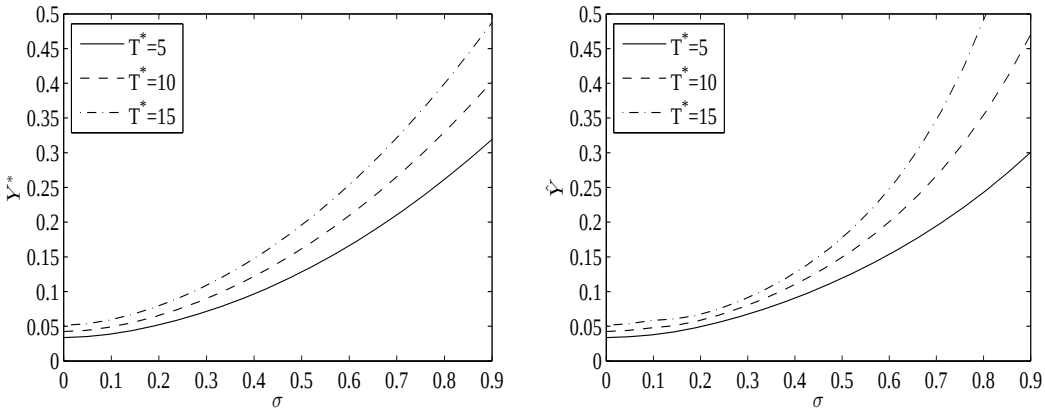
$$F_R^*(\hat{Y})f_R'(\hat{Y}) = (F_R^*(\hat{Y}))'f_R(\hat{Y}). \tag{4.26}$$

To prove the existence and uniqueness in the above conjecture, the sign of "$f'(y)$" (see equation (4.41) in the Appendix) must be determined. The first and second order derivatives of the NPV function for the project that has commercialization flexibility (equation (4.25)) with respect to "y" are the keys to determine the sign. However, due to the complicated functional form of the NPV function, it is impossible to calculate these derivatives. The existence of the investment threshold in the conjecture is based on numerical methods and the uniqueness is based on induction. (see Appendix)

4.5 Comparison of Projects with and without Commercialization Flexibility

Four problems are focused on during the comparisons. First, we discuss how investment thresholds in each project vary with uncertainty σ for different investment lags. Second, we compare how investment thresholds of the two projects vary with uncertainty σ for the same investment lag. Third, to find out which project provides pharmaceutical companies with more incentives to start the R&D process earlier, we compute the probabilities of investments taking place within T years for the two projects. Last, to find out when the products will be available on the market, we calculate the probabilities that commercialization will start at the end of the R&D process.

Figure 4.1 shows how investment thresholds in each project vary with uncertainty for different investment lags. We first compare the investment thresholds within each project.



(a) Without commercialization flexibility (b) With commercialization flexibility

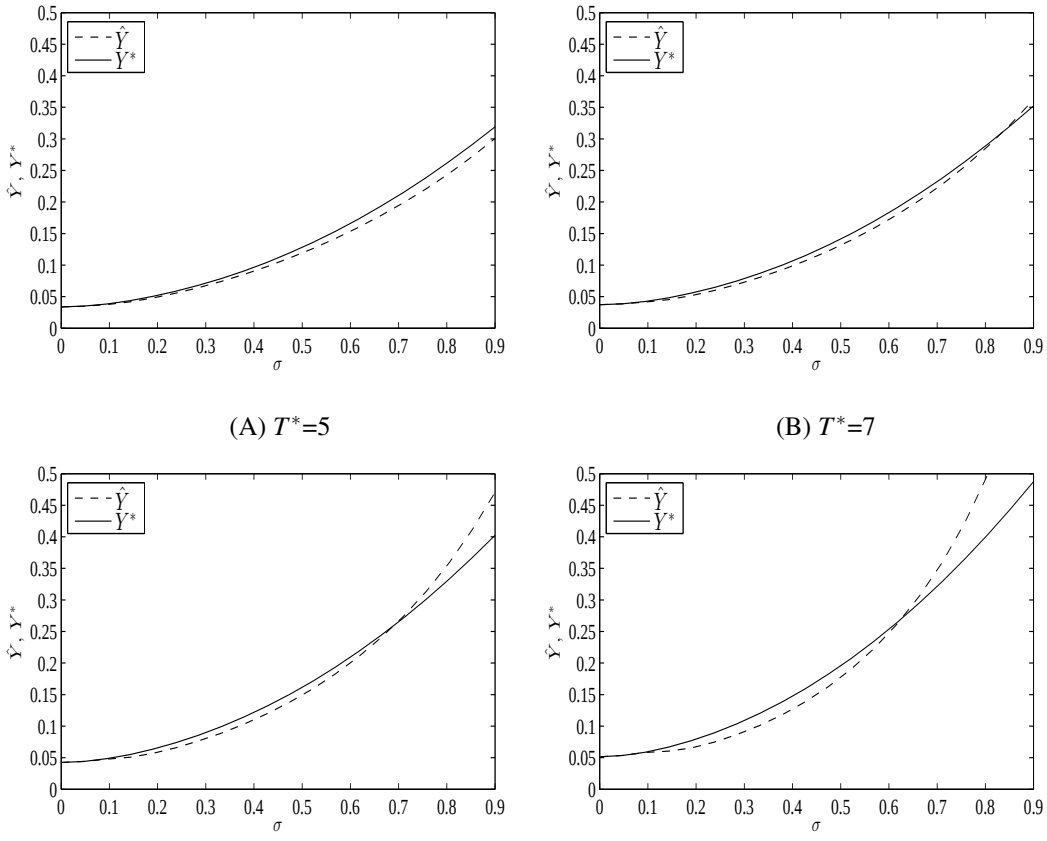
Fig. 4.1 Comparison for the investment thresholds Y^* and $\hat{Y}$ vary with respect to uncertainty σ for different investment lags for each projects. $\hat{Y}$ and Y^* represent the investment thresholds of the project with and without commercialization flexibility respectively. The parameter values are: the discount rate $\rho = 0.05$, the growth rate $\mu = 0.03$, the sunk cost for commercialization $I_c = 0.5$, the cost flows per period during the R&D process $c_R = 0.05$, the uncertainty σ ranges from 0.001 to 0.9 and the investment lag T^* ranges from 5 to 15.

In figure 4.1 (a) and (b) respectively, we notice that the investment thresholds with larger investment lag always dominate the one with smaller investment lag. Intuitively, there are two reasons. First, since it is assumed the costs of the project are paid per period, a larger investment lag or longer R&D process ends up with higher overall costs which reduces the NPV of the investment. In this case, a higher investment threshold is needed to ensure a positive NPV of the project. Moreover, future revenues will be discounted more heavily with a larger investment lag in both projects, which also reduces the NPV of the investments. Second, a higher investment lag T^* leads to higher uncertainty in the value of Y_t at the time of approval. For the project with commercialization flexibility, the option value of commercialization process also increases with higher uncertainty. Both the decrease of NPV and the increase in the option value contribute to a higher investment threshold.

Next, this thesis addresses the second problem by comparing the evolution of investment thresholds between projects in Figure 4.2. In figure (A), the investment threshold of the project with commercialization flexibility is strictly below the other one when the investment lag is 5 years. However, as the investment lag T^* increases from 5 to 7 years, as shown in figure (B), the two thresholds cross out each other when σ is between 0.8 and 0.9. In figure (C) and figure (D), as T^* further increases, the thresholds cross out even sooner when σ is between 0.6 and 0.7.

Before discussing why the thresholds vary in this way, three facts need to be mentioned. (1) The NPV of the project with commercialization flexibility is always greater or equal to the NPV of the project without commercialization flexibility. (2) There are two options in the project with commercialization flexibility, which are the option to defer investment, and the option to defer commercialization; but there is only one option in the project without commercialization flexibility, which is to defer investment. (3) The increase in the uncertainty σ will not influence the NPV of the project with immediate commercialization, while it has effects on the NPV of the project that has commercialization flexibility, since the expected revenues

are only dependent on the growth rate of the stochastic process due to the fact that $E_{Y_t}(Y_{t+T^*}) = Y_t e^{\mu T^*}$.



(A) T^*=5 (B) T^*=7

(C) T^*=10 (D) T^*=15

Fig. 4.2 Comparison for the investment thresholds for different projects with different investment lags. $\hat{Y}$ and Y^* represent the investment thresholds of the project with and without commercialization flexibility respectively. The parameter values are: the discount rate $\rho = 0.05$, the growth rate $\mu = 0.03$, the sunk cost for commercialization $I_c = 0.5$, the cost flows per period during the R&D process $c_R = 0.05$, the uncertainties σ range from 0.001 to 0.9 and the investment lag T^* range from 5 to 15.

Three conclusions can be drawn from the above facts. The first conclusion is when uncertainty $\sigma = 0$, the investment thresholds of both projects are equal. In this case, the commercialization flexibility does not provide with additional value to the project since the expected value of the commercialization process at the approval date is certain. Without uncertainty, the only choice that the investor has is to start the commercialization process right after approval without further delay. Hence the

optimal investment strategy is to invest when NPV>0 since further waiting will only lead to lower overall NPV due to the assumption of $r > \mu$.

The second conclusion is when the investment lag T^* is small and as uncertainty σ goes up, the investment threshold of the project that has commercialization flexibility $\hat{Y}$ increases slower than the threshold of the project without commercialization flexibility. For the project without commercialization flexibility, the increase in σ leads to higher option value while the expected NPV of the project stays the same. Thus the investment threshold of the project goes up.

For the project with commercialization flexibility, an increase in σ does not only increase the value of waiting before investment due to higher volatility of the underlying stochastic process, but also because of the increased NPV of the commercialization process since uncertainty makes the commercialization flexibility valuable. However, since the investment lag T^* is low, for the same length of waiting, for example, T_w years, as σ goes up, the option value increases slower than NPV because the option value of waiting is based on the value of Y_t on time $T_w + T^*$. More specifically, when T^* is much lower than T_w, as σ goes up, the gain from the option value is relatively lower. Since NPV increases faster while the option value increases slower, the investment threshold goes up slower than the one of the project without commercialization flexibility.

The third conclusion is the investment threshold of the project that has commercialization flexibility $\hat{Y}$ increases faster as uncertainty σ goes up with higher investment lag T^*. This conclusion also results from the balance of the NPV and the option value. For the project with immediate commercialization, an increase in σ will increase the option value of investment, which is the same as it is when T^* is small. For the other project, a higher T^* will increase the volatility of Y_t at the approval date, thus the option value of commercialization process also increases. As σ goes up, on one hand, the NPV of the project increases. On the other hand, the option value also increases but it increases faster than the NPV of the project. The reason is, when T^* is larger, for the same length of waiting, for example, T_w years, as σ goes up, the volatility of Y_t which is based on time $T_w + T^*$, is much higher.

When T^* is much higher than T_w, as σ goes up, the gain from the option value is also higher. Since the option value increases faster than NPV, the investment threshold goes up faster than the one of the project without commercialization flexibility.

The third problem that we discuss is which project provides investors with more incentives to start the R&D process earlier. This can be done by either comparing the value of the investment thresholds of the two projects, or more intuitively, by computing the probabilities of investment taking place within a certain amount of time.

Letting $\bar{\mu} = \mu - \frac{1}{2}\sigma^2$, the probability that Y^* is reached within T period equals (Harrison, 1985)

$$P_y\left(\sup_{0\le t\le T} Y_t \ge Y^*\right) = \Phi\left(\frac{-\log\left(\frac{Y^*}{y}\right)+\bar{\mu}T}{\sigma\sqrt{T}}\right) + \left(\frac{Y^*}{y}\right)^{\frac{2\bar{\mu}}{\sigma^2}} \Phi\left(\frac{-\log\left(\frac{Y^*}{y}\right)-\bar{\mu}T}{\sigma\sqrt{T}}\right), \tag{4.27}$$

where $\Phi(\cdot)$ is the cumulative distribution function of the standard normal distribution and y the initial value of the process $(Y_t)_{t\ge 0}$.

For a given volatility, lower investment thresholds are equivalent to earlier investments taking place within certain period. The numerical results show that when σ ranges from 0.2 to 0.6, the project with commercialization flexibility has a higher probability of starting the project than the project with immediate commercialization. However, when σ ranges from 0.7 to 0.9, the values of the two probabilities are reversed.

Lastly, we discuss the probability of the commercialization process taking place by the end of the R&D process. For the project without commercialization flexibility, the probability that the commercialization starts at the end of the R&D process is 1. For the project with commercialization flexibility, we simulate 300,000 sample paths of the underlying stochastic process $(Y_t)_{t\ge 0}$, by choosing the optimal investment threshold $\hat{Y}$ as the initial value. Y_c^*, the optimal commercialization threshold and $Y_{t_R+T^*}$, the value of stochastic process T^* years after starting at $\hat{Y}$, are compared.

The probability of immediate commercialization at the end of the commercialization process is computed as the number of sample paths that end up with $Y_{t_R+T^*} \geq Y_c^*$ divided by 300,000, the total number of simulation. And the probability of delaying commercialization is $1-$ (the probability of immediate commercialization).

How the probabilities change with respect to uncertainty σ and T^* are shown in table 4.1 (See Appendix). As it is shown in the table, the commercialization probabilities decrease with higher σ and increase with higher T^*. Intuitively, when σ goes up, the option value of commercialization goes up. Decision maker tends to defer commercialization until the option value is fully captured before paying the sunk cost which leads to lower commercialization probabilities. When T^* increases, there is a higher probability that the optimal commercialization threshold will be exceeded in expectation, since the growth rate μ of the stochastic process is positive. Thus a higher T^* leads to higher commercialization probability.

In conclusion, the project with commercialization flexibility has a higher probability to start the R&D process as well as commercialization earlier under low uncertainties. Hence it is great for the government to offer commercialization flexibility when uncertainty is low. However, when uncertainty is high, both the probabilities of starting the R&D and commercialization processes are lower, which implies less investment incentives and a longer time before the products are launched. In this case, the government is better off by making immediate commercialization compulsory. Moreover, faster approval policy, which is modeled by a less T^*, works better when σ is lower since the probability of commercialization is negative related to the uncertainty in the revenue process.

4.6 Policy implications

Several policy implications can be drawn from the models.

First, if the priority of the government is to maximize the utility of the expenditure or the total value of the R& D project, commercialization flexibility should always be provided. For the project without commercialization flexibility, at the

approval date, the pharmaceutical company has no option but to commercialize immediately. However, for the other project, the decision maker has the flexibility to decide the timing of the commercialization process, which adds value to the whole project. Thus the value of the project that has commercialization process always dominates the other one, due to the additional option value of the flexibility. Hence if the value of the project is the top concern, the authority should always allow the pharmaceutical companies to decide when to start selling the drugs.

Second, if earlier investment is the priority, for different combination of the uncertainty and the length of the investment lag, two opposite policies should be provided.

On one hand, it is better not to provide with commercialization flexibility for the projects with long investment lag when uncertainty is high. In practice, the reason that a project has longer investment lag could be that the pharmaceutical company is working on a product which is of great therapeutic improvement. For the pharmaceutical company, once these products are launched, the profits are huge since the drugs with great improvements often have the potential to become the "blockbuster drug". Uncertainty can be anything that has great influence on the profitability of the drug. Since "blockbuster drugs" will usually take over the whole market without competitors, when uncertainty is high, it is wise to delay selling the drugs, which will maximize the commercialization process without being worried about similar products launched. In this case, if the authority believes it is necessary to incentivize these companies to launch selling the drugs earlier, commercialization flexibility should not be provided. The earlier the products are commercialized, the higher benefits the patients will get. The option value that is missing because of the policy could be subsidized in ways such as lower tax or price subsidy as a reward for both therapeutic improvement as well as earlier investment.

On the other hand, it is fine to provide pharmaceutical companies with commercialization flexibility when uncertainty is low. The reason is that when uncertainty is low, despite the length of the project, as uncertainty goes up, the NPV of the project that has commercialization flexibility increases faster than the option value. In other

words, the opportunity cost of waiting goes up as uncertainty goes up, which leads to earlier investment. Ultimately, the profitability of immediate investment could be one of the decisive factors regarding whether commercialization flexibility should be allowed or not. In order to incentivize earlier investment, commercialization flexibility should be provided when the opportunity cost of waiting is higher.

4.7 Conclusions

In this chapter, this thesis models a pharmaceutical R&D project under uncertainty where investment decisions are influenced by both investment lag and commercialization flexibility. It is assumed that the end of the R&D process does not necessarily generate the revenues, which is different from many other real options models assuming that the payoffs will be received immediately after the investment lag. Because of the commercialization flexibility, the decision maker is able to choose whether to start commercialization immediately or delay it, dependent on the value of the stochastic process at that time. In this project, the option to start investment is the prerequisite of the option to defer commercialization. Hence the project can also be considered as a compound option with an investment lag, which is new in the literature of evaluation on pharmaceutical R&D projects.

By comparing the two projects, we find that the project with commercialization flexibility provides with more investment incentives when uncertainty is low despite the fact that it always has a higher project value. When uncertainty is low, the option value of commercialization flexibility is low, since the NPV of the project is higher, the investment threshold is lower and the investment probability is higher. When uncertainty is high, the total option value of the project is higher which leads to a higher investment threshold and lower investment probability.

Finally, this thesis discusses the probability of immediate commercialization by the end of the R&D process. For the project without commercialization flexibility, the probability is 1. For the other project, uncertainty will reduce the probability of immediate commercialization since decision maker will want to capture the option

value by waiting further. On the other hand, a higher investment lag will increase the probability of commercialization. Hence, fast approval policy, modeled by a smaller investment lag, is more effective in terms of early commercialization when uncertainty is low.

4.8 Appendix

Proof of Lemma 4.1

(a) Since Y_{t+T^*} follows Geometric Brownian Motion (GBM), $Y_{t+T^*} = Y_t e^{(\mu-\frac{1}{2}\sigma^2)T^*+\sigma B_{T^*}}$, where $B_{T^*} \sim N(0,T^*)$.

Thus the expected value

$$\begin{aligned}
E_{Y_t}(Y_{t+T^*}) =& Y_t e^{(\mu-\frac{1}{2}\sigma^2)T^*} E_t(e^{\sigma B_{T^*}}) \\
=& Y_t e^{(\mu-\frac{1}{2}\sigma^2)T^*} \int_{-\infty}^{\infty} e^{\sigma B_{T^*}} \frac{1}{\sqrt{2\pi T^*}} e^{-\frac{B_{T^*}^2}{2T^*}} dB_{T^*} \\
=& Y_t e^{(\mu-\frac{1}{2}\sigma^2)T^*} \int_{-\infty}^{\infty} \frac{1}{\sqrt{2\pi T^*}} e^{\frac{-(B_{T^*}-T^*\sigma)^2+(T^*)^2\sigma^2}{2T^*}} dB_{T^*} \\
=& Y_t e^{(\mu-\frac{1}{2}\sigma^2)T^*} e^{\frac{\sigma^2 T^*}{2}} \int_{-\infty}^{\infty} \frac{1}{\sqrt{2\pi T^*}} e^{\frac{-(B_{T^*}-T^*\sigma)^2}{2T^*}} dB_{T^*} \\
=& Y_t e^{(\mu-\frac{1}{2}\sigma^2)T^*} e^{\frac{\sigma^2 T^*}{2}} \\
=& Y_t e^{\mu T^*}.
\end{aligned} \tag{4.28}$$

(b) Let $f(Y_{t+T^*}) = (Y_{t+T^*})^{\beta_1}$, by using Ito's lemma we have

$$\begin{aligned}
d(Y_{t+T^*})^{\beta_1} &= (\mu_2 Y \frac{\partial f}{\partial Y} + \frac{1}{2}\sigma^2 Y^2 \frac{\partial^2 f}{\partial Y^2})dt + \sigma Y \frac{\partial f}{\partial Y} dB_t \\
&= \left[\mu\beta_1 + \frac{1}{2}\sigma^2\beta_1(\beta_1-1)\right] Y^{\beta_1} dt + \sigma\beta_1 Y^{\beta_1} dB_t.
\end{aligned} \tag{4.29}$$

Divide equation 4.29 by $f(Y_{t+T^*})$ on both sides, then we have

$$\frac{df(Y_{t+T^*})}{f(Y_{t+T^*})} = \widetilde{\mu} dt + \widetilde{\sigma} dB_t, \tag{4.30}$$

where the parameters $\widetilde{\mu} = \mu\beta_1 + \frac{1}{2}\sigma^2\beta_1(\beta_1-1)$ and $\widetilde{\sigma} = \sigma\beta_1$. So, it is proved that $(Y_{t+T^*})^{\beta_1}$ also follows GBM with a drift $\tilde{\mu}$ and a volatility $\tilde{\sigma}$ if Y_{t+T^*} follows GBM.

By using the result proved in part (a), we know that

$$E_{Y_t}\left[(Y_{t+T^*})^{\beta_1}\right] = (Y_t)^{\beta_1} e^{[\mu\beta_1 + \frac{1}{2}\sigma^2\beta_1(\beta_1-1)]T^*}. \tag{4.31}$$

In conclusion,

$$\begin{aligned} &E_{Y_t}(C(Y_{t+T^*};Y^*)|Y_{t+T^*} < Y^*) = E_{Y_t}\left[(Y_{t+T^*})^{\beta_1}\right](Y^*)^{-\beta_1}(\frac{Y^*}{\rho-\mu} - I_c) \\ &= (Y_t)^{\beta_1} e^{[\mu\beta_1 + \frac{1}{2}\sigma^2\beta_1(\beta_1-1)]T^*}(Y^*)^{-\beta_1}(\frac{Y^*}{\rho-\mu} - I_c) \end{aligned} \tag{4.32}$$

and

$$E_{Y_t}(D(Y_{t+T^*})|Y_{t+T^*} \geq Y^*) = \frac{E_{Y_t}\left(Y_{t+T^*}\right)}{\rho-\mu} - I_c = \frac{Y_t e^{\mu T^*}}{\rho-\mu} - I_c. \tag{4.33}$$

Since Y_{t+T^*} follows GBM,

$$Y_{t+T^*} = Y_t e^{(\mu - \frac{1}{2}\sigma^2)T^* + \sigma B_{T^*}}, \tag{4.34}$$

$\log(\frac{Y_{t+T^*}}{Y_t})$ is normally distributed with expectation $(\mu - \frac{1}{2}\sigma^2)T^*$ and variance $\sigma^2 T^*$, i.e.,

$$\log(\frac{Y_{t+T^*}}{Y_t}) \sim N((\mu - \frac{1}{2}\sigma^2)T^*, \sigma^2 T^*). \tag{4.35}$$

By standardization,

$$\frac{\log(\frac{Y_{t+T^*}}{Y_t}) - (\mu - \frac{1}{2}\sigma^2)T^*}{\sigma\sqrt{T^*}} \sim N(0,1) \tag{4.36}$$

and

$$P_{Y_t}(Y_{t+T^*} < Y^*) = P_{Y_t}(\frac{\log(\frac{Y_{t+T^*}}{Y_t}) - (\mu - \frac{1}{2}\sigma^2)T^*}{\sigma\sqrt{T^*}} < \frac{\log(\frac{Y^*}{Y_t}) - (\mu - \frac{1}{2}\sigma^2)T^*}{\sigma\sqrt{T^*}}), \tag{4.37}$$

which completes the proof. ■

Conjecture 4.1

We first try to prove the existence of at least one solution to the equation (4.26). Since the general solution of $F_R^*(y)$ is Ay^{β_1}, to prove that there is a unique y such that $F_R^*(y)f_R'(y) = (F_R^*(y))'f_R(y)$ holds, we first replace $F_R^*(y)$ with Ay^{β_1}. Thus we have

$$Ay^{\beta_1}f_R'(y) = A\beta_1 y^{\beta_1 - 1}f_R(y) \tag{4.38}$$

$$\Longrightarrow yf_R'(y) = \beta_1 f_R(y) \tag{4.39}$$

$$\Longrightarrow y = \beta_1 \frac{f_R(y)}{f_R'(y)} := f(y) \tag{4.40}$$

If $f(y)$ is an increasing function, according to the Knaster-Tarski fixed-point theorem, there exists at least one y that satisfies $y = f(y)$. Thus the problem is reduced to prove that $f(y)' > 0$.

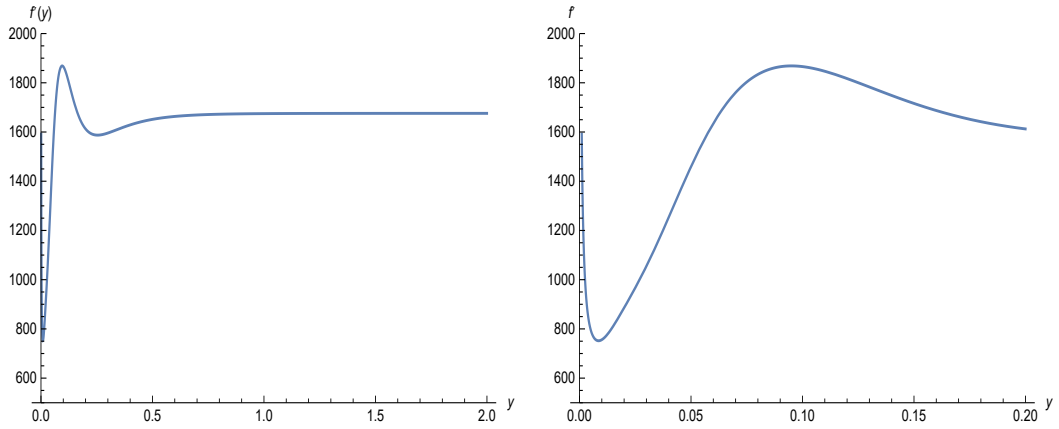
Since

$$f(y)' = \frac{\beta_1\left[(f_R'(y))^2 - f(y)f_R''(y)\right]}{(f_R'(y))^2}, \tag{4.41}$$

$\beta_1 > 1$ and $f'(y)^2 > 0$, we need to prove

$$f_R'(y)^2 - f_R(y)f_R''(y) > 0. \tag{4.42}$$

However, the function f_R (see Equation 4.25) is highly non-linear since it is composed the products of convex functions with cumulative distribution functions (CDF). Hence the derivative f_R' will be even more complicated and it is composed of the products of convex functions, CDF and probability density function (PDF). It is difficult to prove the inequality $f_R'(y)^2 - f_R(y)f_R''(y) > 0$ holds analytically. However, extensive numerical experiments show that the inequality $f_R'(y)^2 - f_R(y)f_R''(y) > 0$ always holds under different parameter values. As Figure 4.3 shows that the minimum value of $f'(y)$ is positive and it stays as a constant when y is large enough.



(a) y ranges from $[0.001, 2]$ (b) y ranges from [0.001, 0.2]

Fig. 4.3 Numerical experiments of $f'(y)$. The parameter values are: the discount rate $\rho = 0.05$, the growth rate $\mu = 0.03$, the sunk cost for commercialization $I_c = 1$, the cost flows per period during the R&D process $c_R = 0.05$, the uncertainties $\sigma = 0.2$ and the investment lag $T^* = 10$.

Next, we try to prove the uniqueness of the solution. Because the NPV function f_R is the weighted average of two convex functions, which are $E_{Y_t}\left(C(Y_{t+T^*}; Y_c^*)|Y_{t+T^*} < Y_c^*\right)$ and $E_{Y_t}\left(D(Y_{t+T_c^*})|Y_{t+T^*} \geq Y_c^*\right)$, and the option value function is simply the expected discounted NPV when the investment optimally takes place. Moreover, since the expected discount factor often takes the form of $f(y)^{\beta_1}$ which is also a convex function. Thus we argue that the value function should be a more convex function than the NPV function where the second order condition is satisfied (Thijssen (2013a)).

Thus we conclude that $f'(y) > 0$ and there is a unique $\hat{Y}$ such that $F_R^*(y)f_R'(y) = (F_R^*(y))'f_R(y)$ holds. ■

Commercialization Probabilities under Different Uncertainty σ and Investment Lag T^*.

Table 4.1 Simulation of the immediate commercialization probabilities. The uncertainty σ changes from 0.1 to 0.9, the growth rate of the stochastic process $\mu = 0.03$, the investment lag $T^* = 5$ and 10 years, the cost of commercialization $I_c = 0.8$, the R&D cost flow of each period $c_R = 0.05$.

σ	$T^* = 5$	$T^* = 10$
0.1	1	1
0.2	0.9985	1
0.3	0.9348	0.9991
0.4	0.8115	0.9777
0.5	0.7134	0.9283
0.6	0.6483	0.8772
0.7	0.6092	0.8356
0.8	0.5866	0.8116
0.9	0.5740	0.7966

Chapter 5

On the Interaction of Government Quality Standards and Pharmaceutical Investment Timing

5.1 Abstract

This chapter discusses how different roles that the government plays in the pharmaceutical R&D projects will help solve the lack of investment problem on Neglected Tropical Diseases (NTDs). There are two types of projects that the government acts within: as a sponsor in the Private-Public Partnership (PPP) with another pharmaceutical company (the decentralized project), or acts as the social planner being in charge of the whole project. It is proved that the optimal investment threshold of the social planner's project is lower and the project value strictly dominates the decentralized project. However, the model also shows that the remuneration level is a great tool to adjust the quality standard of the product in the decentralized project but not in the social planner's project. Policy advices that the social planner's project is a better option if funding is limited since the project starts sooner and leads to higher quality product. The decentralized project is a better choice if funding is

sufficient and a higher quality standard is the priority.

5.2 Introduction

Seventeen kinds of NTDs, classified by the World Health Organization (WHO), cause severe pain, long-term disability, and are the cause of death for over 500,000 people per year.[1] It is estimated that more than 1 billion people suffer from at least one NTD (WHO (2015)). Most often, the people affected by these tropical diseases are living in the poorest developing countries, which are suffering from poor sanitation, lack of clean water, and necessary health care. The diseases, which cause high mortality and morbidity among the people, are traditionally neglected in the pharmaceutical industry for mainly two reasons. First, people affected by these tropical diseases have a low profile and status in public health priorities, and lack a strong political voice.[2] Second, the pharmaceutical industry has little incentive to invest in R&D for the diseases that predominantly plague poor nations, as medicines cannot be sold there at a price that would allow pharmaceutical firms to cover their high R&D costs (Buckup (2008)). It is found that, of 1393 new chemical entities marketed between 1975 and 1999, only 16 were for tropical diseases and tuberculosis. There is a 13-fold greater chance of a drug being brought to market for central-nervous-system disorders or cancer than for a neglected disease (Trouiller et al. (2002)).

In order to tackle the lack of investment incentives problem, governments, non-profit organizations (NPOs) and foundations have been contributing substantial funds to help increase the investments on the R&D projects that deal with NTDs. Various favorable marketing conditions, including research grants, public support for clinical trials (Yamey (2002)), are granted to encourage pharmaceutical companies to enter into public-private partnership (PPP). With the support of the public organizations,

[1]The END (Ending Neglected Diseases) fund. http://www.end.org/whatwedo/ntdoverview

[2]World Health Organization (WHO) Q&A, Why are some tropical diseases called “neglect”? http://www.who.int/features/qa/58/en/

investment intentions of the pharmaceutical companies in the R&D projects that deal with NTDs may increase. Since pharmaceutical investment is subject to substantial uncertainty on future market conditions, one of the proposed mechanisms to deal with this uncertainty in the public-private partnership is via Advance Purchase Commitments (APC).

These are commitments, by the public organizations such as the governments or NPOs, "to purchase specified 'technologies' in specified 'quantities' in the 'future' at a 'guaranteed' unit 'price' " (Farlow (2004) [quotation mark in the original]). Despite the many disadvantages of this mechanism as discussed by Farlow (2004), it is widely accepted that APCs are one of the best ways to finance R&D projects for neglected diseases (Levine et al. (2005)).

Another way of solving the lack of investment problem is that the government will be responsible for the drug development on its own instead of cooperating with privates firms. Giesecke (2000) compared the science and technology (S&T) policies of Germany and the US and showed that direct interventionist S&T policy did not necessarily lead to successful innovations. Despite the effort that the German government has made, such as initiating working groups, advisory boards, and funding programs for the advancement of biotech research, it turned out that "enabling a preferable economic ecology for biotech development was more successful than an interventionist policy."

However, this does not help much if the priority now is not to develop a self-growing market for battling NTDs in a long run, but to have sufficient projects which are able to produce high quality drugs to cure the affected people in the short run since most of the NTDs can be "eliminated". For instance, Malaria is not coming back to the developed countries where it has been effectively wiped out. The priority is to choose a project that starts as soon as possible, produces high quality drugs and has higher project value with same costs.

In this chapter, which role the government should play in the drug development is discussed by comparing two projects with different managerial structures. In the first project, an advance purchase commitments contract is signed between the

government and a biopharmaceutical company. The contract states that once the drug produced by the biopharmaceutical company meets a quality standard set by the government, a fixed amount of money will be paid to the company. In the second project, the government plays the role of a social planner and is responsible for the research, production and marketing of the drug on its own. More often than not, the drug development projects have the following features. First, the costs are irreversible; second, the investment timing is flexible; last, the cash flows are uncertain. The real options approach is a good choice in evaluating these projects since it captures all these features.

The analysis in the comparison of the two projects is similar to the vertical control problem in the industrial organization literature, regarding the relationship of an "upstream firm" and a "downstream firm" (Tirole (1988)). In the decentralized project, the government is similar to the role of the downstream firm since it purchases the products from the pharmaceutical company, and then sells them to the consumers. In the IO literature, however, the upstream firm usually moves first by selling the intermediate products to the downstream firms, and then to the retailers (downstream firm). Then after transformation of the intermediate products, the retailers sell the final products to consumers.

In terms of welfare analysis, we show that the integrated project or the social planner's project has a higher overall project value, which is similar to the result of Spengler (1950). He argues that the vertical structure is more profitable under vertical integration than under a linear price since the monopoly profit of the vertical structure is realized. The social welfare is increased due to the elimination of the "double marginalization" problem. However, in this model, the effects of the prices and demands of the intermediate and final product are not considered, the different projects' values are only dependent on the quality of the product. The reason for a higher value for the integrated project is because the maximization problems that the government and the pharmaceutical company solve are constrained, while the problem the social planner solves is unconstrained.

There are four main findings of this chapter. First, it shows that the optimal investment threshold of the social planner's project is strictly lower than the decentralized project. In other words, the social planner's project will always start sooner. Second, if the budget for remuneration is limited while the sunk cost of the project is relatively low, a social planner's project is a better option since the project not only starts sooner but also ends up with higher quality standard. Third, if there is sufficient funding to afford higher remuneration, the remuneration level can be used as an effective tool to adjust the quality standard of the product. However, increasing the remuneration level could also lead to a delay in commercialization. Last, the social planner's project has a higher project value than the decentralized one and this fact is independent of the key parameters of the model, such as discount rate, growth rate and uncertainty.

The remainder of the chapter is organized as follow. Section 5.3 introduces decentralized project. Section 5.4 discusses the project run by the social planner. In section 5.5, the values of the two projects are compared. Section 5.6 considers policy implications. Finally, section 5.7 concludes the chapter.

5.3 The Decentralized R&D Project

Consider a pharmaceutical company that is provided with an opportunity to invest in developing a drug. The investment is irreversible and subject to a sunk cost $I > 0$ which is paid at the start of the project. To ensure the future market and incentivize the company to invest, an advance purchase commitments contract is signed between the government and the company specifying: (1) The quality standard of the drug, which is often set by the industry and sponsors together and (2) The revenues of the project, which will be paid as a constant cash flow R per period infinitely, if the quality standard is met. In practice, the cash flows will only be paid for a certain period of time. However, with a finite horizon, the expected discounted value of the cash flows simply equals to the value of infinite cash flows multiply by a discount

factor, which can be easily applied. For analytical convenience, we assume the cash flows are infinite here.

When the project is finished, there would be an independent adjudication committee (IAC), with primary responsibility for determining whether the product meets the technical specification (Berndt and Hurvitz (2005)). The pre-specified quality standard is denoted by q_c^A in the model. Like many other R&D projects, there exist investment lags. In other words, the sunk cost will be paid long before receiving revenues in the future since it takes time to reach the quality standard.

Every pharmaceutical project can be considered as a series of sub-projects and is composed of several nodes including pre-discovery, discovery, pre-clinical, phase I, II and III and approval (Hartmann and Hassan (2006)). In order to focus on the problems that we are interested in the chapter, we simplify the project by combining the phases mentioned above into two major phases: the research phase before incurring a great amount of costs, which includes pre-discovery, discovery, pre-clinical phases and the development phase after paying the sunk cost, which includes the three phases of clinical trials (Paul et al. (2010)).

The uncertainty in revenues is dependent on the quality of the product which is modeled by a geometric Brownian motion (GBM) $(q_t)_{t\geq 0}$. The quality of the product mentioned in this chapter is an abstract indicator of the most probable reasons of failures of the R&D process, such as lack of efficacy and safety issues confirmed by Arrowsmith and Miller (2013) and Cook et al. (2014). As the R&D process continues, more information will be collected as how to improve both efficacy and safety of the products, which will update the previous knowledge about the quality of the product as a whole. GBM is a great tool to model such a situation where the trend of the quality is positive subject to fluctuations as more information gathered during the drug development process. In the research phase, the manufacturer will conduct researches including "Target-to-hit", "Hit-to-lead", "Lead-to-optimization" and "pre-clinical trials" with lower costs in order to collect as much information favorable to the development phase later. According to Paul et al. (2010), the total cost of the development phase greatly out weights that of the

research phase. Without loss of generality, we assume the cost of the research phase is 0. However, the quality of the product will only be slightly improved during this phase, which evolves according to the SDE,

$$dq_t = \mu_1 q_t dt + \sigma q_t dB_t, \tag{5.1}$$

where B_t is a Wiener process and q_t has initial value q, $P-a.s.$

Once the manufacturer considers the product promising, the development phase starts and the sunk cost I will be paid, which will boost up the quality of the product in a greater speed and the process is denoted by,

$$dq_t = \mu_2 q_t dt + \sigma q_t dB_t, \tag{5.2}$$

where $0 < \mu_1 < \mu_2$.

In conclusion, let τ be the time of investment. Then

$$dq_t = \begin{cases} \mu_1 q_t dt + \sigma q_t dB_t & if \quad t < \tau \\ \mu_2 q_t dt + \sigma q_t dB_t & if \quad t \geq \tau. \end{cases} \tag{5.3}$$

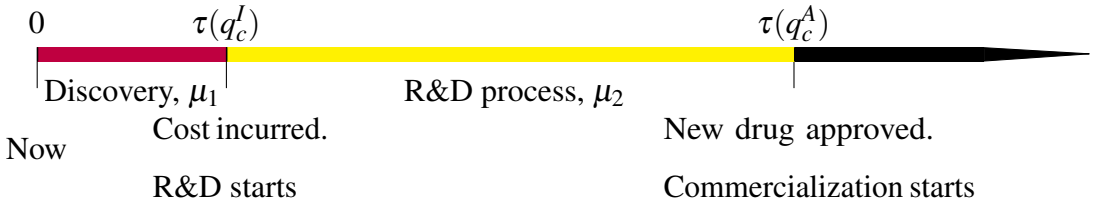
Although the pharmaceutical companies usually do not have priors for the average qualities in both the research and development phases (μ_1 and μ_2), the idea of setting $\mu_1 < \mu_2$ is to model a more intensive development stage, in which the product has greater probability of success so that the quality increases faster after paying the sunk cost. This assumption is more realistic for phase 1 and 3 trials in that if the product has ever reached these stages, the transitional probabilities are 54% and 70% (Paul et al. (2010)). For phase 2 trial, the probability is estimated to be 34%. Moreover, it is assumed that both trends are non-negative in that, to focus on the choice of organizational structures and simplify the investment problems, the projects are assumed to be successful with probability 1 if they last long enough.

Consider the following dynamic game with two players: the government and a pharmaceutical company. The government moves first by specifying a quality standard q_c^A. Once q_c^A is reached, a constant cash flow R will be paid to the pharmaceutical company forever. The pharmaceutical company moves next by choosing the optimal time τ to start the project and pay the sunk cost. The firm stops further development of the product once q_c^A is reached.

It is worth noting that the cash flow R can also be modeled as q_c^A multiply by some price p which will lead to the same conclusions in the chapter, since instead of setting the cash flow per period equal to a constant R, the government can always find a constant p that makes the product of p and q_c^A equal to R. For analytical convenience, we use R.

5.3.1 The Pharmaceutical Company's Problem

The time line of the project is as follows:



Once q_c^A is reached, the government will need to fulfill the advance purchase commitments by paying a constant cash flow R to the pharmaceutical company. The production cost that incurred by the company is denoted by C, a fixed cost flow per period for infinity and it is assumed that $R > C$. In addition, the decision makers are assumed to be risk neutral and that ρ is the discount rate of firm and government. The NPV of commercialization when q_c^A being reached is:

$$\begin{aligned} f(q_c^A) &= \int_0^\infty e^{-\rho t}(R-C)dt \\ &= \frac{R-C}{\rho}. \end{aligned} \tag{5.4}$$

The stopping time of which the investment of the development phase becomes optimal is denoted by τ. As in most of the real options literature, the optimal stopping time takes the form of the first hitting times of some threshold q_c^I. For $q^* > 0$, denote the first passage time of q^* by $\tau(q^*) := \inf\{t \geq 0 \mid q_t \geq q^*\}$. Thus the optimal time of investment is $\tau(q_c^I)$. In addition, denote $\tau_s(q^*) := \inf\{t \geq s \mid q_t \geq q^*\}$ and the subscript is omitted when $s = 0$. So, $\tau_{\tau(q_c^I)}(q_c^A)$ is the random time, starting from the time of investment, that the quality standard is met. Thus $\tau(q_c^A) = \tau(q_c^I) + \tau_{\tau(q_c^I)}(q_c^A)$ and revenues will accrue from this point onwards.

The firm's problem is to solve the optimal stopping problem:

$$\begin{aligned} V^S(q) &= \sup_{\tau(q_c^I)} E_q \left[\int_{\tau(q_c^I)+\tau_{\tau(q_c^I)}(q_c^A)}^{\infty} e^{-\rho t}(R-C)dt - e^{-\rho\,\tau(q_c^I)} I \right] \\ &= \sup_{q_c^I} E_q \left\{ e^{-\rho\,\tau(q_c^I)} E_{q_c^I} \left[\int_{\tau_{\tau(q_c^I)}(q_c^A)}^{\infty} e^{-\rho t}(R-C)dt - I \right] \right\} \\ &= \sup_{q_c^I} E_q \left\{ e^{-\rho\,\tau(q_c^I)} E_{q_c^I} \left[e^{-\rho\,\tau_{\tau(q_c^I)}(q_c^A)} E_{q_c^A} \left(\int_0^{\infty} e^{-\rho t}(R-C)dt \right) - I \right] \right\} \\ &\equiv \sup_{q_c^I} E_q \left[e^{-\rho\,\tau(q_c^I)} F(q_c^I) \right], \end{aligned} \tag{5.5}$$

where

$$\begin{aligned} F(q_c^I) &= E_{q_c^I} \left[e^{-\rho\,\tau_{\tau(q_c^I)}(q_c^A)} E_{q_c^A} \left(f(q_c^A) \right) \right] - I \\ &= E_{q_c^I} \left[e^{-\rho\,\tau_{\tau(q_c^I)}(q_c^A)} f(q_c^A) \right] - I. \end{aligned} \tag{5.6}$$

The first line of equation 5.5 shows that the pharmaceutical company wants to maximize the expected revenues accruing from time $\tau(q_c^A)$ by paying the sunk cost I at time $\tau(q_c^I)$. And $\tau_{\tau(q_c^I)}(q_c^A)$ is the first time that q_t hits q_c^A after starting the project. The equations that follow are further derivations by using the Markovian property of the stochastic process $(q_t)_{t\geq 0}$. The last line is to formalize the problem into the one that can be solved by the standard real options approach.

We first need to compute the value of $F(q_c^I)$. Since $f(q_c^A)$ is a constant, it can be taken out of the expectation and we obtain

$$F(q_c^I) = E_{q_c^I}[e^{-\rho\tau_{\tau(q_c^I)}(q_c^A)}]f(q_c^A) - I. \tag{5.7}$$

The characteristic operator of the process q_t after investment is

$$\mathscr{L}_q\varphi = \frac{1}{2}\sigma^2 q^2\frac{\partial^2\varphi}{\partial q^2} + \mu_2 q\frac{\partial\varphi}{\partial q}. \tag{5.8}$$

The general solution of the equation $\mathscr{L}_q\varphi = \rho\varphi$ is of the form,

$$\varphi(q) = Aq^{\beta_1(\mu_2)} + Bq^{\beta_2(\mu_2)}, \tag{5.9}$$

where $\beta_1(\mu_2) > 1$ and $\beta_2(\mu_2) < 0$ are the two roots of the quadratic equation,

$$\mathscr{Q}_2(\beta) = \frac{1}{2}\sigma^2\beta(\beta-1) + \mu_2\beta - \rho = 0. \tag{5.10}$$

The boundary condition $\varphi(0) = 0$ can only be satisfied iff $B = 0$ which gives $\varphi(q) = Aq^{\beta_1(\mu_2)}$ on (q_c^I, q_c^A). For now, we assume that $q_c^I < q_c^A$.

By using Dynkin's formula, the expected discount factor is

$$E_{q_c^I}[e^{-\rho\tau_{\tau(q_c^I)}(q_c^A)}] = \frac{\varphi(q_c^I)}{\varphi(q_c^A)} = \left(\frac{q_c^I}{q_c^A}\right)^{\beta_1(\mu_2)}. \tag{5.11}$$

So the value of $F(q_c^I)$ is

$$\begin{aligned} F(q_c^I) &= \left(\frac{q_c^I}{q_c^A}\right)^{\beta_1(\mu_2)} f(q_c^A) - I \\ &= \left(\frac{q_c^I}{q_c^A}\right)^{\beta_1(\mu_2)} \left(\frac{R-C}{\rho}\right) - I. \end{aligned} \tag{5.12}$$

By using the same approach above again, we are able to compute the expected discount factor,

$$E_q\left[e^{-\rho\tau(q_c^I)}\right] = \left(\frac{q}{q_c^I}\right)^{\beta_1(\mu_1)}, \tag{5.13}$$

where $\beta_1(\mu_1) > 1$ is one of the two roots of the quadratic equation,

$$\mathscr{Q}_1(\beta) = \frac{1}{2}\sigma^2\beta(\beta-1) + \mu_1\beta - \rho = 0. \tag{5.14}$$

Proposition 5.1 *The project value for the pharmaceutical company is:*

$$V^S(q) = \begin{cases} \left(\frac{q}{q_c^I}\right)^{\beta_1(\mu_1)}\left[\left(\frac{q_c^I}{q_c^A}\right)^{\beta_1(\mu_2)}\left(\frac{R-C}{\rho}\right) - I\right] & if \quad q < q_c^I \\ \left(\frac{q}{q_c^A}\right)^{\beta_1(\mu_2)}\left(\frac{R-C}{\rho}\right) - I & if \quad q_c^I \leq q < q_c^A \\ \frac{R-C}{\rho} & if \quad q \geq q_c^A \end{cases} \tag{5.15}$$

From the perspective of the pharmaceutical company, the value of the project at any point in time is dependent on the value of the stochastic process $(q_t)_{t\geq 0}$, which represents the quality of the product at that time. If the product's quality is less than the optimal investment threshold q_c^I, the best strategy is to stay in the discovery phase, wait and observe the evolution of $(q_t)_{t\geq 0}$, and pay the sunk cost as soon as q_c^I is reached. If the product's quality is larger or equal to q_c^I, but less than the pre-specified quality q_c^A, the best strategy is to invest and start the development phase immediately. Finally, if the quality is larger or equal to q_c^I, there is no point in staying in the research phase or starting the development phase, the best strategy of the pharmaceutical company is to start commercialization process immediately by paying the operating cost C per period.

Proposition 5.2 *q_c^I is the optimal investment threshold that maximizes the pharmaceutical company's project value and $q_c^I = q_c^A\left[\frac{\beta_1(\mu_1)}{\beta_1(\mu_1)-\beta_1(\mu_2)}\frac{\rho I}{R-C}\right]^{1/\beta_1(\mu_2)}$.*

See proof of the proposition in the Appendix.

Lemma 5.1 *The ratio* $\frac{\beta_1(\mu_1)}{\beta_1(\mu_1)-\beta_1(\mu_2)} > 1$*, which ensures that the investment threshold* q_c^I *is non-negative.*

See proof of lemma 5.1 in the Appendix.

In addition, to ensure proposition 5.2 makes economic sense, it is assumed that $\frac{\beta_1(\mu_1)}{\beta_1(\mu_1)-\beta_1(\mu_2)} < \frac{R-C}{\rho I}$, therefore, $q_c^I < q_c^A$. This condition will need to be satisfied so that the pharmaceutical company will have incentive to start the project in the first place. Otherwise, conducting basic research in the discovery phase without paying any costs will lead to a successful product.

5.3.2 The Government's Problem

In the previous section, we have computed the optimal investment threshold of the pharmaceutical company which is shown in proposition 5.2. For each quality standard set by the government, the pharmaceutical company will come up with a unique corresponding optimal investment threshold. Since there is no hidden information between the two players, the government knows that the quality standard will be set under the condition that the equation $q_c^I = q_c^A \left[\frac{\beta_1(\mu_1)}{\beta_1(\mu_1)-\beta_1(\mu_2)} \frac{\rho I}{R-C}\right]^{1/\beta_1(\mu_2)}$ is a common knowledge. Moreover, since the government is the first mover in the game, the pharmaceutical company will have to accept the quality standard given and adjusts its strategies accordingly. Mathematically, q_c^I is a function of q_c^A and it will be replaced by using q_c^A in the calculation of the government's optimal quality standard.

The objective of the government is to set an optimal quality standard q_c^A to maximize the present value of patients' health gain net of payment to the firm. Suppose the patients' overall health is linearly dependent on the quality of the product, which is represented by $B(q_c^A) = Kq_c^A$, where $K > 0$. The problem of the

government is then:

$$\begin{aligned}
V^F(q) &= \sup_{q_c^A} E_q \left[\int_{\tau(q_c^I)+\tau_{\tau(q_c^I)}(q_c^A)}^{\infty} e^{-\rho t}(Kq_c^A - R)dt \right] \\
&= \sup_{q_c^A} E_q \left\{ e^{-\rho\,\tau(q_c^I)} E_{q_c^I} \left[\int_{\tau_{\tau(q_c^I)}(q_c^A)}^{\infty} e^{-\rho t}(Kq_c^A - R)dt \right] \right\} \\
&= \sup_{q_c^A} E_q \left\{ e^{-\rho\,\tau(q_c^I)} E_{q_c^I} \left[e^{-\rho\,\tau_{\tau(q_c^I)}(q_c^A)} E_{q_c^A} \left(\int_0^{\infty} e^{-\rho t}(Kq_c^A - R)dt \right) \right] \right\} \\
&= \sup_{q_c^A} \left\{ \left(\frac{q}{q_c^I} \right)^{\beta_1(\mu_1)} E_{q_c^I} \left[e^{-\rho\,\tau_{\tau(q_c^I)}(q_c^A)} v(q_c^A) \right] \right\}, \qquad (5.16)
\end{aligned}$$

where

$$\begin{aligned}
v(q_c^A) &= \int_0^{\infty} e^{-\rho t}(Kq_c^A - R)dt \\
&= \frac{Kq_c^A - R}{\rho}. \qquad (5.17)
\end{aligned}$$

In the above equations, the Markovian property of the stochastic process $(q_t)_{t\geq 0}$ is used again by treating the time to start the project $\tau(q_c^I)$ and the approval time $\tau(q_c^A)$ as new beginnings.

By using the same approach in the last section, we are able to compute the expected discount factor,

$$E_{q_c^I} \left[e^{-\rho\,\tau_{\tau(q_c^I)}(q_c^A)} \right] = \left(\frac{q_c^I}{q_c^A} \right)^{\beta_1(\mu_2)}. \qquad (5.18)$$

As in the problem of the pharmaceutical company, the government's problem can be rewritten as:

$$\begin{aligned}
V^F(q) &= \sup_{q_c^A} \left\{ \left(\frac{q}{q_c^I} \right)^{\beta_1(\mu_1)} E_{q_c^I} \left[e^{-\rho\,\tau_{\tau(q_c^I)}(q_c^A)} \right] v(q_c^A) \right\} \\
&= \sup_{q_c^A} \left\{ \left(\frac{q}{q_c^I} \right)^{\beta_1(\mu_1)} \left(\frac{q_c^I}{q_c^A} \right)^{\beta_1(\mu_2)} v(q_c^A) \right\}. \qquad (5.19)
\end{aligned}$$

Proposition 5.3 *The project value for the government is*

$$V^F(q) = \begin{cases} \left(\frac{q}{q_c^I}\right)^{\beta_1(\mu_1)} \left[\left(\frac{q_c^I}{q_c^A}\right)^{\beta_1(\mu_2)} \left(\frac{Kq_c^A - R}{\rho}\right)\right] & if \quad q < q_c^I \\ \left(\frac{q}{q_c^A}\right)^{\beta_1(\mu_2)} \left(\frac{Kq_c^A - R}{\rho}\right) & if \quad q_c^I \leq q < q_c^A \\ \frac{Kq - R}{\rho} & if \quad q \geq q_c^A \end{cases} \tag{5.20}$$

The value of the government's project is dependent on the current quality of the product. If the current quality $q < q_c^I$, the pharmaceutical company will stay in the discovery phase and wait until the optimal investment threshold is reached before investment. After investment, the development phase continues till the optimal quality standard is met which is the time the payoff of the government is realized. If the current quality $q_c^I \leq q < q_c^A$, the pharmaceutical company will start the development phase immediately and the payoff is realized when the optimal quality standard is met. Lastly, if $q \geq q_c^A$, the quality of the product has exceeded the optimal quality standard. Hence the government can launch selling the product immediately.

Proposition 5.4 *q_c^A is the optimal quality standard that maximizes the government's project value and $q_c^A = \frac{\beta_1(\mu_1)}{\beta_1(\mu_1)-1}\frac{R}{K}$. Replacing q_c^A in the value of q_c^I in proposition 5.2, we have*

$$q_c^I = \frac{\beta_1(\mu_1)}{\beta_1(\mu_1)-1}\frac{R}{K}\left[\frac{\beta_1(\mu_1)}{\beta_1(\mu_1)-\beta_1(\mu_2)}\frac{\rho I}{R-C}\right]^{1/\beta_1(\mu_2)}. \tag{5.21}$$

See proof of proposition 5.4 in the Appendix.

Since the government's willingness to pay is a constant, the only decision that the pharmaceutical company will have to make is when to start investment regardless of the timing of commercialization. In this case, when the quality standard q_c^A is reached, the products are commercialized immediately. And for the government, the only decision to make is how a quality standard q_c^A is supposed to be set which maximizes patients' health gains net of payoffs to the firm, conditional on the

reaction function of the pharmaceutical company being a common knowledge to both players. The unique pair of strategies that maximize the project values of both players is (q_c^A, q_c^I) . The uniqueness is due to both the optimal thresholds are satisfying value matching and smooth pasting conditions (Dixit and Pindyck, 1994).

5.4 The Social Planner's R&D Project

In the decentralized R&D project, the pharmaceutical company and the government are both involved and each of them is in charge of only part of the project. The government is charge of the commercialization process and it moves first by setting a quality standard of the final product. The pharmaceutical company is in charge of the research and development of the product. Dependent on the quality standard, it moves next by choosing the best time to start the development phase. The goal of each player is to maximize the project value that each of them being in charge of .

Now consider the project is taken over by a social planner who will be in charge of both R&D and commercialization. In this case, the decision of investment and how to set the optimal quality standard will need to be considered simultaneously. The goal of the social planner is to maximize the project value as a whole.

The optimal investment threshold and the optimal quality standard are denoted by q_I^I and q_I^A, respectively, in the social planner's project. The problem of the social planner is:

$$\begin{aligned} V^I(q) &= \sup_{q_I^A, q_I^I} E_q \left[\int_{\tau(q_I^A)}^{\infty} e^{-\rho t} (B(q_I^A) - C) dt - I e^{-\rho \tau(q_I^I)} \right] \\ &= \sup_{q_I^A, q_I^I} \left\{ \left(\frac{q}{q_I^I} \right)^{\beta_1(\mu_1)} \left[\left(\frac{q_I^I}{q_I^A} \right)^{\beta_1(\mu_2)} \left(\frac{K q_I^A - C}{\rho} \right) - I \right] \right\} \end{aligned} \tag{5.22}$$

The investment problem can be solved by treating q_I^A as a constant and taking the partial derivatives of $V^I(q)$ with respect to q_I^I.

And $\frac{\partial V^I(q)}{\partial q_I^I} = 0$ gives

$$q_I^I = q_I^A \left(\frac{\beta_1(\mu_1)}{\beta_1(\mu_1) - \beta_1(\mu_2)} \frac{\rho I}{K q_I^A - C} \right)^{1/\beta_1(\mu_2)}. \tag{5.23}$$

The problem of what quality standard to be set in order to maximize the social welfare can be solved by taking partial derivatives of $V^I(q)$ with respect to q_c^A.

And $\frac{\partial V^I(q)}{\partial q_c^A} = 0$ gives

$$q_I^A = \frac{\beta_1(\mu_2)}{\beta_1(\mu_2) - 1} \frac{C}{K}. \tag{5.24}$$

Replacing q_I^A in equation 5.23, we have

$$q_I^I = \frac{\beta_1(\mu_2)}{\beta_1(\mu_2) - 1} \frac{C}{K} \left[\frac{\beta_1(\mu_1)}{\beta_1(\mu_1) - \beta_1(\mu_2)} (\beta_1(\mu_2) - 1) \frac{\rho I}{C} \right]^{1/\beta_1(\mu_2)}. \tag{5.25}$$

In addition, to ensure equation 5.23 makes economic sense, it is assumed that $q_I^I \leq q_I^A$. Thus, the condition

$$C > \frac{\beta_1(\mu_1)(\beta_1(\mu_2) - 1)}{\beta_1(\mu_1) - \beta_1(\mu_2)} \rho I \tag{5.26}$$

must be satisfied.

Proposition 5.5 *The value of project run by the social planner $V^I(q)$ is maximized if the development phase starts at q_I^I and the quality standard is set to be q_I^A.*

See proof of proposition 5.5 in the Appendix.

Proposition 5.6 *The project value of the social planner is*

$$V^I(q) = \begin{cases} \left(\frac{q}{q_I^I}\right)^{\beta_1(\mu_1)} \left[\left(\frac{q_I^I}{q_I^A}\right)^{\beta_1(\mu_2)} \left(\frac{K q_I^A - C}{\rho}\right) \right] & if \quad q < q_I^I \\ \left(\frac{q}{q_I^A}\right)^{\beta_1(\mu_2)} \left(\frac{K q_I^A - C}{\rho}\right) & if \quad q_I^I \leq q < q_I^A \\ \frac{Kq - C}{\rho} & if \quad q \geq q_I^A \end{cases} \tag{5.27}$$

The project value of the social planner is dependent on the quality of the product. If the current quality is less than the optimal investment threshold i.e., $q < q_I^I$, the social planner will consider stay in the discovery phase, wait and collect more information and invest until the quality is high enough. If the current quality is higher than the optimal investment threshold but lower than the optimal quality standard i.e., $q_I^I \leq q < q_I^A$, the social planner will skip the discovery phase and start the development phase immediately. The development phase will be finished until the optimal quality standard is first met. Lastly, if the current quality is larger than the optimal quality standard i.e., $q \geq q_I^A$, both the research and development phase can be skipped. The best strategy is to start commercialization right away.

5.5 Analysis of Thresholds and Project Values

All together, this thesis has introduced four different thresholds for the two projects. They are: (1) q_c^I, the optimal investment threshold of the decentralized project, (2) q_c^A, the optimal quality standard set by the government in the decentralized project, (3) q_I^I, the optimal investment threshold of the project run by the social planner and (4) q_I^A, the optimal quality standard set by the social planner.

In order to make the investment problems more interesting, in both projects, we assume that the optimal investment thresholds are less than the optimal quality standards. Otherwise, the quality standard will be reached within the research phase without starting the development phase which is usually unrealistic in reality.

More specifically, in the decentralized project, we assume that $q_c^I < q_c^A$. The corresponding condition to be satisfied is

$$R > \frac{\beta_1(\mu_1)}{\beta_1(\mu_1) - \beta_1(\mu_2)} \rho I + C. \tag{5.28}$$

In the project run by the social planner, we assume that $q_I^I < q_I^A$. The corresponding condition to be satisfied is

$$C > \frac{\beta_1(\mu_1)(\beta_1(\mu_2)-1)}{\beta_1(\mu_1)-\beta_1(\mu_2)}\rho I. \tag{5.29}$$

Next, we discuss the relation of the two optimal investment thresholds.

Proposition 5.7 *The investment threshold of the social planner's project q_I^I, is strictly less than that of the decentralized project q_c^I, i.e., $q_I^I < q_c^I$.*

See proof of Proposition 5.7 in the Appendix.

To show the difference of the two investment thresholds in a more intuitive way, we present a numerical example when the parameter values are $\mu_1 = 0.02$, $\mu_2 = 0.2$, $\sigma = [0.001, 0.9]$, $I = 10$, $\rho = 0.5$, $C = 20$, $K = 100$ and $R = 80$. Figure 5.1 shows the investment threshold of the project is strictly dominated when run by the social planner. Given that the growth rates μ_1, μ_2 and the volatility σ of the stochastic process $(q_t)_{t\geq 0}$ are the same for both projects, smaller investment threshold means sooner investment and start of the development phase.

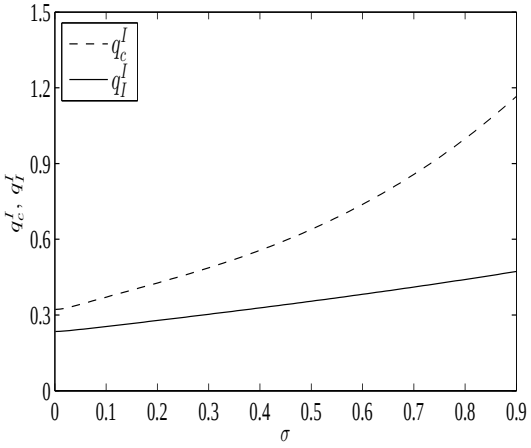


Fig. 5.1 The difference of investment thresholds as uncertainty varies.

Intuitively, the difference of the investment threshold lies in the different organizational structure of the two projects. In the decentralized project, there are two players whose goals are to maximize their own project values. From the perspective of the government, for a certain quality standard, the sooner the investment takes place, the higher the payoffs; and an earlier investment means the product will be finished sooner due to higher growth rate and there will be less discounting on the

value of patients' wealth gain. However, from the perspective of the pharmaceutical company, earlier investment means giving up the information and the chance to improve of the quality of product during the discovery phase. In order to capture the option value in the discovery phase, the pharmaceutical company will tend to wait and invest when the quality of the product is high enough.

However, for the project run by the social planner, the objective of the social planner is to maximize the project value as a whole. Both investment timing and quality standard are considered simultaneously. For the same quality standard, earlier investment helps sooner realization of patients' health gain, which is consistent with the benefit of the social planner. Although earlier investment benefits the government in the decentralized project, it does not necessarily benefit the pharmaceutical company. The conflict between the two players in the decentralized project leads to late investment. Hence the investment threshold in the social planner's project is lower without conflicts.

A noticeable difference between the two projects is that the pharmaceutical company will receive a renumeration R from the government by the end of the development phase in the decentralized project if the product is successful. However, in the project run by the social planner, the variable R does not exist.

Next, the effects that the renumeration level has on the different thresholds in the decentralized project and the relation of the optimal quality standards in different projects because of R is analyzed.

For computational convenience, denote M as the right hand side of the inequality 5.28, i.e., $M = \frac{\beta_1(\mu_1)}{\beta_1(\mu_1)-\beta_1(\mu_2)}\rho I + C$, and denote $N = \frac{(\beta_1(\mu_1)-1)\beta_1(\mu_2)}{(\beta_1(\mu_2)-1)\beta_1(\mu_2)}C$.

Proposition 5.8 *When* $0 < I < \frac{(\beta_1(\mu_1)-\beta_1(\mu_2))^2 C}{\beta_1(\mu_1)^2(\beta_1(\mu_2)-1)\rho}$, $M < N$. *If* $M < R < N$, *the optimal quality standard of the decentralized project is less than the one run by the social planner i.e.,* $q_c^A < q_I^A$. *Hence,* $q_I^I < q_c^I < q_c^A < q_I^A$.

See proof of Proposition 5.8 in the Appendix.

The optimal quality standard of the social planner q_I^A is not affected by the variations of remuneration level since there is no remuneration in the social planner's

project. However, a lower remuneration level will lead to a lower quality standard in the decentralized project q_c^A (See Proposition 5.4). The sunk cost does not affect the quality standards of both projects directly. In the social planner's project, the decrease in the sunk cost will lead to a lower required operating cost (see equation 5.29), which does not have any influence on the quality standard if the operating cost is high enough. Similarly, the quality standard of the decentralized project q_c^A is indirectly affected by the sunk cost. A lower sunk cost will lead to a lower required remuneration (see Equation 5.28). However, as long as the minimum requirement of R is satisfied, i.e., if equation 5.28 holds, the sunk cost I will not influence the quality standard of the decentralized project. The proposition shows that when R is low, the optimal quality standard of the decentralized project is less than the one run by the social planner. Policy advices that if the budget for remuneration is limited while the sunk cost of the project is relatively low, a social planner's project is preferred since the project will not only be started sooner, which means the products will be finished and commercialized sooner, the quality standard of the project is also higher.

Proposition 5.9 *When* $0 < I < \frac{(\beta_1(\mu_1)-\beta_1(\mu_2))^2 C}{\beta_1(\mu_1)^2(\beta_1(\mu_2)-1)\rho}$, $M < N$ *and when* $I \geq \frac{(\beta_1(\mu_1)-\beta_1(\mu_2))^2 C}{\beta_1(\mu_1)^2(\beta_1(\mu_2)-1)\rho}$, $M \geq N$. *If* $R \geq \max\{M,N\}$, *the optimal quality standard of the project run by the social planner is less or equal to the one of the decentralized project, i.e.,* $q_I^A \leq q_c^A$. *Moreover, there is a unique remuneration level* R_c (R_{cc}) *such that the optimal investment threshold of the decentralized project equals the optimal quality standard of the social planner's project, i.e.,* $q_c^I = q_I^A$. *Thus if* $N(M) \leq R < R_c(R_{cc})$, $q_I^I < q_c^I < q_I^A < q_c^A$. *If* $R \geq R_c(R_{cc})$, $q_I^I < q_I^A \leq q_c^I < q_c^A$.

See proof of Proposition 5.9 in the Appendix.

By increasing the remuneration level, the result in Proposition 5.8 can be reversed. When $R \geq \max\{M,N\}$, the quality standard of the decentralized project q_c^A increases while the quality standard of the social planner's project q_I^A is not affected. Moreover, as R goes up, the investment threshold of the decentralized project q_c^I first goes down then goes up. When $N(M) \leq R < R_c(R_{cc})$, the investment threshold

of the decentralized project is less than the quality standard of the social planner's project, i.e., $q_c^I < q_I^A$. If R further increases, when $R \geq R_c(R_{cc})$, the investment threshold of the decentralized project will be larger or equal to the quality standard of the social planner's project, i.e., $q_c^I \geq q_I^A$.

With sufficient funding, the remuneration level R can be used as a tool to adjust the quality standard of the product in the decentralized project, which is not possible for the social planner's project. However, this is with the cost that the product will be commercialized later since q_c^I will be increasing with R as well. In an extreme case, for instance, when R takes values in $R \geq R_c(R_{cc})$, it may be that the final product in the social planner's project has been finished while the development phase has not even started in the decentralized project.

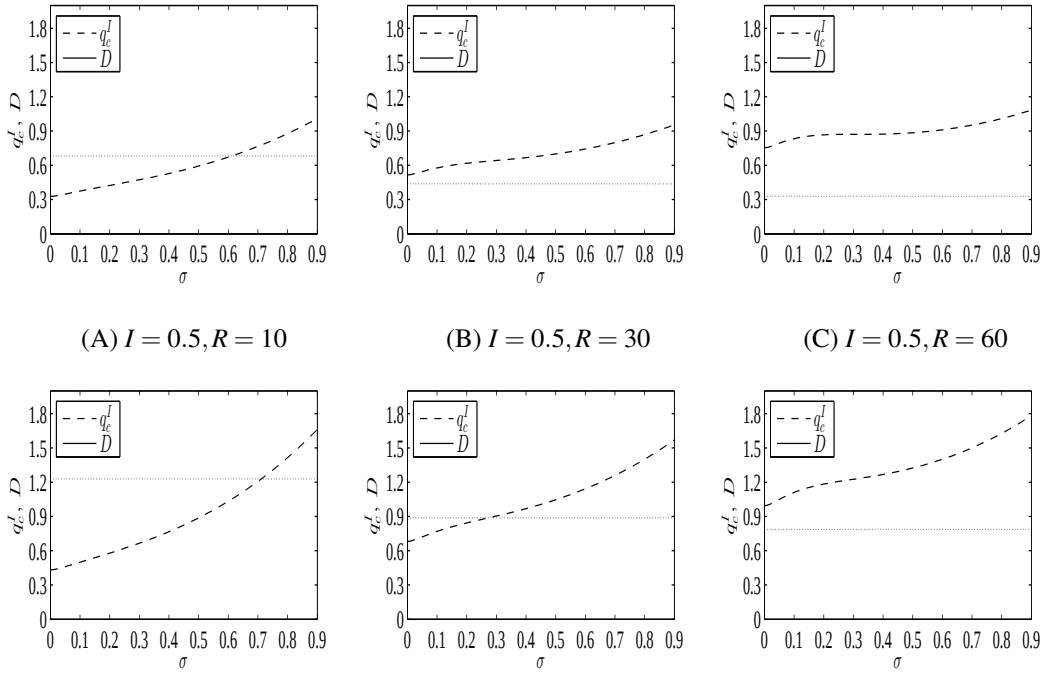
Moreover, it can be proved that $R_{cc} \leq R_c$. In other words, the higher the sunk cost I, the less remuneration R is required to make q_c^I approaches q_I^A from below. Mathematically, this is because q_c^I increases with I while q_I^A is not affected if the operating cost C reaches the minimum value, i.e., $C > \frac{\beta_1(\mu_1)(\beta_1(\mu_2)-1)}{\beta_1(\mu_1)-\beta_1(\mu_2)}\rho I$.

Next, in Figure 5.2, we analyze how investment threshold of the decentralized project vary with uncertainty and how the spread of the maximum and minimum value of the threshold changes under different sunk costs and level of remunerations.

Proposition 5.10 *The spread of the maximum and minimum value of the investment threshold under different uncertainties decreases when the remuneration level R increases. And the spread increases with increasing sunk cost I.*

The investment threshold of the decentralized project increases with uncertainty. Moreover, as the remuneration level R increases, the spread of the maximum and minimum value of the investment threshold decreases. The effect of R on the investment threshold q_c^I can be separated into two parts. From Proposition 5.4, we know that $q_c^I = \frac{\beta_1(\mu_1)}{\beta_1(\mu_1)-1}\frac{R}{K}\left[\frac{\beta_1(\mu_1)}{\beta_1(\mu_1)-\beta_1(\mu_2)}\frac{\rho I}{R-C}\right]^{1/\beta_1(\mu_2)}$ which can be considered as a product of two terms. First, an increase in R will lead to higher quality standard since $q_c^A = \frac{\beta_1(\mu_1)}{\beta_1(\mu_1)-1}\frac{R}{K}$. This is quite intuitive since a product with higher quality often requires more input of the available resources such as time, money and

effort. To increase the incentives of consuming more resources on the research and development of a product, a higher remuneration level will be needed. The influence that the remuneration level R has on the optimal quality standard q_c^A is the "quality effect" and this effect will tend to delay the investment decision. Second, an increase in R means higher future revenues and thus, decision maker will want to receive the revenues sooner. We call the influence that R has on the NPV of the project the "NPV effect" which encourages earlier investment and is captured in the term $\left[\frac{\beta_1(\mu_1)}{\beta_1(\mu_1)-\beta_1(\mu_2)}\frac{\rho I}{R-C}\right]^{1/\beta_1(\mu_2)}$.



(A) $I = 0.5, R = 10$ (B) $I = 0.5, R = 30$ (C) $I = 0.5, R = 60$

(D) $I = 1, R = 10$ (E) $I = 1, R = 30$ (F) $I = 1, R = 60$

Fig. 5.2 The investment threshold of the decentralized project changes with uncertainty and the spread of the maximum and minimum value of the investment threshold under different sunk costs I and remuneration level R. The parameter values are: $\mu_1 = 0.02$, $\mu_2 = 0.2$, $\sigma = [0.001, 0.9]$, $I = 0.5$ or 1, $\rho = 0.5$, $C = 5$, $K = 10$ and R=10, 30 or 60. In the figures above, D represents the difference of the maximum and minimum value of the investment threshold.

Figure 5.2 shows that when uncertainty is low, the investment threshold goes up faster when R increases. Intuitively, as R goes up, the quality standard goes up. If uncertainty is low, the chances that large upward jumps happen less often. In

this case, a better strategy will be to wait in the discovery phase and invest after the upward jumps are realized, instead of investing earlier and hoping that the upward jumps will happen during the development phase which will lead to sooner finish. Earlier investment means giving up the upward jumps for free, especially when these jumps are more valuable when uncertainty is low since they happen less often. Since the the upward jumps are more valuable when uncertainty is low, it is more important to capture them by investing later when the current quality is higher, which is represented by a higher optimal investment threshold. In other words, the "quality effect" is larger when R goes up with lower uncertainty. Although the "NPV effect" tends to encourage sooner investment, it is limited by the "quality effect". Sooner investment reduces the value of the project when uncertainty is low since the valuable upward jumps are given up. The stronger "quality effect" when uncertainty is low makes the optimal investment threshold goes up faster.

When uncertainty is high, the "quality effect" is weaker since even if earlier investment means giving up the upward jumps in the discovery phase for free, it is more likely that these jumps will happen in the development phase. Hence it is less important to guarantee that the benefits of upward jumps must be captured before investment. And these jumps are less valuable in the sense that they happen more often. Moreover, "NPV effect" is stronger since sooner investment is a possibility. The combination of the two effects leads to slower increase in the threshold when R goes up with higher uncertainty.

Since the "quality effect", which leads to the increase of the investment threshold, is much stronger when uncertainty is low while the "NPV effect", which reduces the investment threshold, becomes stronger when uncertainty is higher, the spread of the maximum and minimum value of the investment threshold decreases as the remuneration level R increases. Moreover, the spread is also related to the value of sunk cost. The higher the sunk cost, the higher the spread. This is because the "NPV effect" is even weaker when I is large while the "quality effect" is not affect. The combination of the two effects makes the spread larger.

Next we compare the value of the decentralized project with the social planner's project.

Proposition 5.11 *The value of the project run by the social planner is greater than the decentralized one.*

See the calculations and comparisons of project values in the Appendix.

Two examples are provided to show the difference of the project values. Figure 5.3 shows the different project values when the start value of the stochastic process q is smaller than the investment thresholds of both projects, i.e., $q < q_I^I < q_c^I$. The parameter values are: $q = 0.3$, $\mu_1 = 0.02$, $\mu_2 = 0.2$, $\sigma = [0.001, 0.9]$, $I = 0.5$, $\rho = 0.5$, $C = 5$, $K = 10$, $R = 7$. In this case, the best strategy of both decision maker is to wait until each investment threshold is reached before paying the sunk cost. It is shown that the value of the social planner's project is strictly larger than the decentralized one.

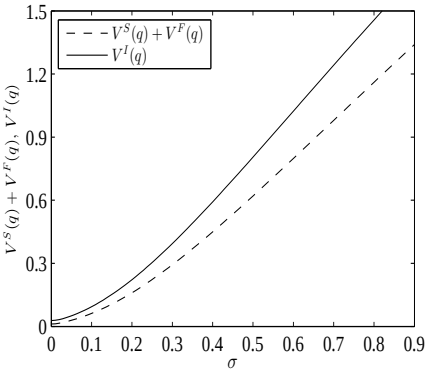


Fig. 5.3 The difference of project values as uncertainty varies, when $q < q_I^I < q_c^I$.

Intuitively, although optimal decisions are made in both projects, the maximization problem that q_I^I solves is an unconstrained one, while q_c^I solves a constrained maximization problem, in which the pharmaceutical company moves next for a given quality standard set by the government in advance. In this case, the option value of the pharmaceutical company's project cannot be fully captured, which leads to the lower total value of the decentralized project. In addition, as uncertainty σ goes up, the value of the decentralized project increases slower which also proves that part of the option value is not captured when uncertainty increases, since the decision of pharmaceutical company is limited by the action of the government.

Figure 5.4 shows the different project values when the start value of the stochastic process q is larger than the investment thresholds of both projects, i.e., $q_I^I < q_c^I < q$. The parameter values are: $q = 2$, $\mu_1 = 0.02$, $\mu_2 = 0.2$, $\sigma = [0.001, 0.9]$, $I = 1$,

$\rho = 0.5$, $C = 5$, $K = 10$, $R = 20$. In this case, both projects will start immediately without further waiting and it is shown that the social planner's project value is strictly larger than the decentralized one.

In this case, the decision made by the government is also affected by the response of the pharmaceutical company in the decentralized project. In other words, the government, although moves first by setting a quality standard, also solves a constrained maximization problem restricted by what the pharmaceutical company will react given the quality standard set. Thus the optimal investment threshold q_c^A does not maximize the unconstrained value function NPV(x) (see Appendix). Hence the total value of the decentralized project is less than the social planner's project. In addition, as uncertainty goes up, both project values decrease. This is because both projects have no flexibilities but to invest immediately at this point. Without options of waiting, the bad outcomes cannot be avoided, thus increasing uncertainty reduces the value of both projects.

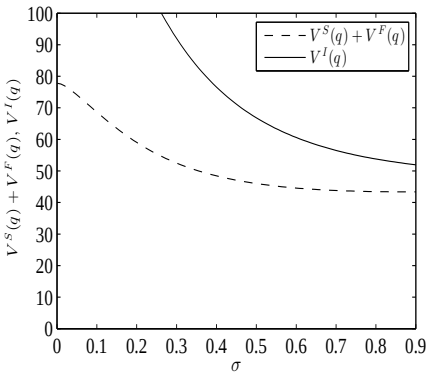


Fig. 5.4 The difference of project values as uncertainty varies, when $q_I^I < q_c^I < q$.

5.6 Policy implications

Several policy implications can be drawn from the model.

First, the social planner's project better suits the development of drugs for the NTDs. The greatest problem of NTDs is not about the quality of the products but the problem of being lack of investment to start the corresponding projects in the first place. Compared with the projects that are financed by using advance purchase commitments (APCs), the social planner's project considers both the decisions of earlier investment and the quality of the product at the same time. Also it is proved that the social planner's project tends to start earlier or has greater probability of

starting the project within certain amount of time under all parameter values, which is exactly what the patients are in great need of.

Second, the decentralized project, which is financed by advance purchase commitments, is a better managerial structure in terms of adjusting the quality of the product. More specifically, a higher remuneration level, which is agreed by both parties before investments, will lead to higher quality of the drug. However, the investment will also be delayed. Moreover, when the remuneration level is below certain threshold, the social planner's project does not only start sooner so that it has the potential of providing patients with earlier treatments, but also makes higher quality of the product. In this case, the social planner's project is the best option. Thus the managerial structure to be chosen is dependent on the budget constraint of the authority. In a word, if the budget of the authority is limited, the social planner's project should be chose. If there is no budget constraint, dependent on whether the priority is an earlier investment or the quality of drug, both social planner's project and the decentralized project are possible.

5.7 Conclusions

In this chapter, we analyze how structural difference will help address the lack of investment incentives in the R&D projects for NTDs. Dependent upon the roles the government plays in different projects, we compare the decentralized project and the social planner's project. In the decentralized project, the government is both a regulator, who determines the quality standard of the product, and a sponsor, who agrees to purchase the final product if the quality standard is met. The pharmaceutical company is the "policy taker" whose only decision is to optimally start the development phase, given the quality standard set by the government. In the social planner's project, the government is in charge of the whole project by setting the optimal quality standard as well as considering the optimal investment timing. The different roles that government play in the two projects have led to several different results.

The comparison of the two models shows that the optimal investment threshold of the social planner's project is strictly less than the one of the decentralized project and the social planner's project will always start sooner. Since we assume that the growth rate will increase dramatically after investment, i.e., $\mu_2 > \mu_1$, the project with sooner investment will also finish sooner in expectation. Thus the social planner's project is a better choice if the unmet clinical needs are required to satisfied in a short time.

Subsequently, we analyze the effect of the remuneration level R on the optimal investment threshold of the decentralized project. It is found that the social planner's project is a better choice in terms of sooner start and higher optimal quality standard, if the sunk cost of the project is relatively low and the sponsor does not have enough funding for remuneration. On the other hand, with sufficient funding, remuneration can be used as a great tool to adjust the quality standard, which is not achievable in the social planner's project. However, the increase in the quality standard also means late commercialization. Thus, the decentralized project is more suitable for the purpose of developing a product with higher quality and is not in urgent. For instance, if a project aims to develop a more effective product for certain disease to replace the current one, the decentralized project will be a better choice in that the quality standard can be easily controlled by setting different remuneration level, while this is impossible for the social planner's project.

Furthermore, we discuss how investment threshold of the decentralized project varies with uncertainty under different remuneration levels and sunk costs. The results show that the investment threshold increases faster as the remuneration level increases with lower uncertainty. This is because the upward jumps are more valuable in the sense they happen less often when uncertainty is low, and it is more important to capture the jumps before investment. Hence as the remuneration level goes up, which leads to higher quality standard, the investment threshold of the decentralized project goes up faster under lower uncertainty than under higher uncertainty.

A possible extension of the model is to endogenize the remuneration level R in the decentralized project. In practice, an endogenized R is more reasonable since the revenues that the company will receive are limited by some budget constraint of the government and should be determined by the maximization problems of both parties. However, two problems will occur if the revenue R is endogenized.

First, if the value function of the government is to be maximized regarding both the quality of the product q_c^A and the revenue R, there will be no closed form solution of R (see equation 5.20), since q_c^I is a nonlinear function of R (see proposition 5.2).

Second, if R is endogenized, although the value of the decentralized project is maximized, the remuneration level will no longer serve as a useful tool to adjust the quality standard of the project. Moreover, as it has been proved that, under the same budget constraint, the centralized project has greater value no matter what. In other words, if the objective is to maximize the value of the project, the decentralized project will never be an optimal choice.

Thus this chapter uses an exogenous R which, on one hand, avoids the problem of not getting a closed form solution of R if it is endogenized. On the other hand, an exogenous R provides the decentralized project with the opportunity to shine when the quality standard instead of the value of the project being the priority of patients and the government.

Finally, it is proved that the value of the social planner's project strictly dominates the decentralized project. Because the problem that the social planner solves is an unconstrained maximization problem while the problems of the pharmaceutical company and the government are two constrained maximization problems. Hence the sum of the two players' project values is less than the social planner's project value.

5.8 Appendix

Proof of Lemma 5.1

We start by looking at the quadratic equation:

$$\mathscr{Q}(\beta) = \frac{1}{2}\sigma^2\beta(\beta-1) + \mu\beta - \rho = 0. \tag{5.30}$$

$\beta_1 > 0$ is one of the two roots of the above equation.

Implicit differentiation of $\mathscr{Q}(\beta_1) = 0$ with respect to μ gives

$$\frac{\partial \mathscr{Q}(\beta_1)}{\partial \beta_1}\frac{\partial \beta_1}{\partial \mu} + \frac{\partial \mathscr{Q}(\beta_1)}{\partial \mu} = 0 \Leftrightarrow \frac{\partial \beta_1}{\partial \mu} = -\frac{\partial \mathscr{Q}(\beta_1)/\partial \mu}{\partial \mathscr{Q}(\beta_1)/\partial \beta_1}. \tag{5.31}$$

The denominator can be computed easily since the graph of $\mathscr{Q}(\beta)$ is a U-shape parabola and $\partial \mathscr{Q}(\beta_1)/\partial \beta_1 > 0$.

From the direct derivatives

$$\frac{\partial \mathscr{Q}(\beta_1)}{\partial \mu} = \beta_1 > 0. \tag{5.32}$$

So it follows that

$$\frac{\partial \beta_1}{\partial \mu} < 0. \tag{5.33}$$

Since we assume that $\mu_1 < \mu_2$, $\beta_1(\mu_1) > \beta_1(\mu_2)$, so

$$\frac{\beta_1(\mu_1)}{\beta_1(\mu_1) - \beta_1(\mu_2)} = 1 + \frac{\beta_1(\mu_2)}{\beta_1(\mu_1) - \beta_1(\mu_2)}. \tag{5.34}$$

Since $\beta_1(\mu_1) > \beta_1(\mu_2)$, $\beta_1(\mu_1) - \beta_1(\mu_2) > 0$,

$$\frac{\beta_1(\mu_1)}{\beta_1(\mu_1) - \beta_1(\mu_2)} > 1. \tag{5.35}$$

■

Proof of Proposition 5.2

The optimal quality threshold can be computed by taking the first order derivatives of equation 5.15 with respect to q_c^I when $q \leq q_c^I$

$$\begin{aligned}\frac{\partial V^S(q)}{\partial q_c^I} =& -\beta_1(\mu_1) q^{\beta_1(\mu_1)} (q_c^I)^{-\beta_1(\mu_1)-1} \left[\left(\frac{q_c^I}{q_c^A} \right)^{\beta_1(\mu_2)} \left(\frac{R-C}{\rho} \right) - I \right] \\ &+ q^{\beta_1(\mu_1)} (q_c^I)^{-\beta_1(\mu_1)} \left[\beta_1(\mu_2) (q_c^I)^{\beta_1(\mu_2)} \left(\frac{R-C}{\rho} \right) \right] \end{aligned} \tag{5.36}$$

and $\frac{\partial V^S(q)}{\partial q_c^I} = 0$ gives

$$q_c^I = q_c^A \left[\frac{\beta_1(\mu_1)}{\beta_1(\mu_1) - \beta_1(\mu_2)} \frac{\rho I}{R-C} \right]^{1/\beta_1(\mu_2)}. \tag{5.37}$$

The second order derivative of equation 5.15 with respect to q_c^A is

$$\begin{aligned}\frac{\partial^2 V^S(q)}{\partial^2 q_c^I} =& q^{\beta_1(\mu_1)} (q_c^I)^{-\beta_1(\mu_1)-2} \Bigg[\beta_1(\mu_1)(\beta_1(\mu_1) \\ &- \beta_1(\mu_2)) \left(\frac{q_c^I}{q_c^A} \right)^{\beta_1(\mu_2)} \left(\frac{R-C}{\rho} \right) - \beta_1(\mu_2)(\beta_1(\mu_2)+1) I \Bigg]. \end{aligned} \tag{5.38}$$

Substituting $\left(\frac{q_c^I}{q_c^A} \right)^{\beta_1(\mu_2)}$ with $\frac{\beta_1(\mu_1)}{\beta_1(\mu_1)-\beta_1(\mu_2)} \frac{\rho I}{R-C}$,

$$\begin{aligned}&\frac{\partial^2 V^S(q)}{\partial^2 q_c^I} \\ =& q^{\beta_1(\mu_1)} (q_c^I)^{-\beta_1(\mu_1)-2} \Bigg[\beta_1(\mu_1)(\beta_1(\mu_1) - \beta_1(\mu_2)) \frac{\beta_1(\mu_1)}{\beta_1(\mu_1) - \beta_1(\mu_2)} \frac{\rho I}{R-C} \frac{R-C}{\rho} \\ &- (\beta_1(\mu_1)+1)\beta_1(\mu_1) I \Bigg] \\ =& q^{\beta_1(\mu_1)} (q_c^I)^{-\beta_1(\mu_1)-2} \Big[-\beta_1(\mu_1) I \Big]. \end{aligned} \tag{5.39}$$

Since $q^{\beta_1(\mu_1)} > 0$ and $(q_c^I)^{-\beta_1(\mu_1)-2} > 0$, $\frac{\partial^2 V^S(q)}{\partial^2 q_c^I} < 0$. q_c^I is the the optimal investment threshold that maximizes the pharmaceutical company's project value. ■

Proof of Proposition 5.4

The optimal quality threshold can be computed by taking the first order derivatives of the value function in Proposition 5.3, when $q < q_c^I$, with respect to q_c^A, and substituting q_c^I with $q_c^I = q_c^A \left[\frac{\beta_1(\mu_1)}{\beta_1(\mu_1)-\beta_1(\mu_2)} \frac{\rho I}{R-C}\right]^{1/\beta_1(\mu_2)}$ as it is in Proposition 5.2,

$$\begin{aligned}\frac{\partial V^F(q)}{\partial q_c^A} =& q^{\beta_1(\mu_2)} \left[\frac{\beta_1(\mu_1)}{\beta_1(\mu_1)-\beta_1(\mu_2)} \frac{\rho I}{R-C}\right]^{\frac{\beta_1(\mu_2)-\beta_1(\mu_1)}{\beta_1(\mu_2)}} \\ & \times \left[-\beta_1(\mu_2)(q_c^A)^{-\beta_1(\mu_2)-1}\left(\frac{Kq_c^A-R}{\rho}\right) + (q_c^A)^{-\beta_1(\mu_2)}\frac{K}{\rho}\right]. \end{aligned} \tag{5.40}$$

For computational convenience, denote

$$M = q^{\beta_1(\mu_2)} \left[\frac{\beta_1(\mu_1)}{\beta_1(\mu_1)-\beta_1(\mu_2)} \frac{\rho I}{R-C}\right]^{\frac{\beta_1(\mu_2)-\beta_1(\mu_1)}{\beta_1(\mu_2)}}. \tag{5.41}$$

$\frac{\partial V^F(q)}{\partial q_c^A}$ can be rewritten as

$$\frac{\partial V^F(q)}{\partial q_c^A} = M\left[-\beta_1(\mu_2)(q_c^A)^{-\beta_1(\mu_2)-1}\left(\frac{Kq_c^A-R}{\rho}\right) + (q_c^A)^{-\beta_1(\mu_2)}\frac{K}{\rho}\right] \tag{5.42}$$

and $\frac{\partial V^F(q)}{\partial q_c^A} = 0$ gives

$$q_c^A = \frac{\beta_1(\mu_1)}{\beta_1(\mu_1)-1}\frac{R}{K}. \tag{5.43}$$

The second order derivative of equation 5.19 with respect to q_c^A is

$$\frac{\partial^2 V^F(q)}{\partial^2 q_c^A} = M(q_c^A)^{-\beta_1(\mu_2)-2}\left[\beta_1(\mu_2)(\beta_1(\mu_2)+1)\frac{Kq_c^A-R}{\rho} - \frac{2Kq_c^A}{\rho}\beta_1(\mu_2)\right]. \tag{5.44}$$

Since $q_c^A = \frac{\beta_1(\mu_2)}{\beta_1(\mu_2)-1}\left(\frac{C}{K}\right)$,

$$\begin{aligned}
&\beta_1(\mu_2)(\beta_1(\mu_2)+1)\frac{Kq_c^A-R}{\rho} - \frac{2Kq_c^A}{\rho}\beta_1(\mu_2)\\
=&\beta_1(\mu_2)(\beta_1(\mu_2)-1)\frac{Kq_c^A}{\rho} - \beta_1(\mu_2)(\beta_1(\mu_2)+1)\frac{R}{\rho}\\
=&\beta_1(\mu_2)(\beta_1(\mu_2)-1)\frac{K}{\rho}\frac{\beta_1(\mu_2)}{\beta_1(\mu_2)-1}\frac{R}{K} - \beta_1(\mu_2)(\beta_1(\mu_2)+1)\frac{R}{\rho}\\
=&-\frac{R}{\rho}\beta_1(\mu_2) < 0.
\end{aligned} \tag{5.45}$$

Because M and q_c^A are both positive, $\frac{\partial^2 V^F(q)}{\partial^2 q_c^A} < 0$.

And it can also be proved that q_c^A maximizes the value function shown in the Proposition 5.3, when $q_c^I \le q < q_c^A$.

$$\frac{\partial V^F(q)}{\partial q_c^A} = (-\beta_1(\mu_2))\left(\frac{q}{q_A^c}\right)^{\beta_1(\mu_2)}\left(\frac{1}{q_c^A}\right)\left(\frac{Kq_c^A-R}{\rho}\right) + \left(\frac{q}{q_A^c}\right)^{\beta_1(\mu_2)}\frac{K}{\rho} \tag{5.46}$$

and $\frac{\partial V^F(q)}{\partial q_c^A} = 0$ gives

$$q_c^A = \frac{\beta_1(\mu_1)}{\beta_1(\mu_1)-1}\frac{R}{K}. \tag{5.47}$$

The first order condition then becomes,

$$\frac{\partial V^F(q)}{\partial q_c^A} = \left(\frac{q(\beta_1(\mu_2)-1)K}{\beta_1(\mu_2)R}\right)^{\beta_1(\mu_2)}\left(\frac{R}{(\beta_1(\mu_2)-1)\rho}\right) > 0. \tag{5.48}$$

The second order condition is,

$$\frac{\partial^2 V^F(q)}{\partial^2 q_c^A} =(-\beta_1(\mu_2))\left(\frac{q}{q_c^A}\right)^{\beta_1(\mu_2)}\left(\frac{1}{q_c^A}\right)\left[(1-\beta_1(\mu_2))\frac{K}{\rho}+\frac{\beta_1(\mu_2)R}{q_A^c\rho}\right] + \left(\frac{q}{q_c^A}\right)^{\beta_1(\mu_2)}\left(-\frac{1}{(q_c^A)^2}\frac{\beta_1(\mu_2)R}{\rho}\right). \tag{5.49}$$

When $q_c^A = \frac{\beta_1(\mu_1)}{\beta_1(\mu_1)-1}\frac{R}{K}$,

$$\frac{\partial^2 V^F(q)}{\partial^2 q_c^A} = \left(\frac{q}{q_c^A}\right)^{\beta_1(\mu_2)}\left(-\frac{\beta_1(\mu_2)R}{(\beta_1(\mu_2)-1)K}\right) < 0 \tag{5.50}$$

Thus q_c^A is the optimal quality standard which maximizes the value of the government's project. ■

Proof of the Proposition 5.5

The partial derivatives of $V^I(q)$ in equation 5.22 with respect to q_I^I is

$$\frac{\partial V^I(q)}{\partial q_I^I} =q^{\beta_1(\mu_1)}(q_I^I)^{\beta_1(\mu_2)-\beta_1(\mu_1)-1}(q_I^A)^{-\beta_1(\mu_2)}\left(\frac{Kq_I^A-C}{\rho}\right)(\beta_1(\mu_2)-\beta_1(\mu_1)) + q^{\beta_1(\mu_1)}(q_I^I)^{-\beta_1(\mu_1)-1}\beta_1(\mu_1)I \tag{5.51}$$

and $\frac{\partial V^I(q)}{\partial q_I^I} = 0$ gives $q_I^I = q_I^A\left(\frac{\beta_1(\mu_1)I}{\beta_1(\mu_1)-\beta_1(\mu_2)}\frac{\rho}{Kq_I^A-C}\right)^{1/\beta_1(\mu_1)}$.

The partial derivatives of $V^I(q)$ with respect to q_I^A is

$$\frac{\partial V^I(q)}{\partial q_I^A} =q^{\beta_1(\mu_1)}(q_I^I)^{\beta_1(\mu_2)-\beta_1(\mu_1)} \times\left[-\beta_1(\mu_2)(q_I^A)^{-\beta_1(\mu_2)-1}\left(\frac{Kq_I^A-C}{\rho}\right)+(q_I^A)^{-\beta_1(\mu_2)}\frac{K}{\rho}\right] \tag{5.52}$$

and $\frac{\partial V^I(q)}{\partial q_I^A} = 0$ gives $q_I^A = \frac{\beta_1(\mu_2)}{\beta_1(\mu_2)-1}\left(\frac{C}{K}\right)$.

The second partial derivatives of $V^I(q)$ with respect to q_I^I is:

$$\begin{aligned}
\frac{\partial^2 V^I(q)}{(\partial q_I^I)^2} =& q^{\beta_1(\mu_1)}(\beta_1(\mu_2)-\beta_1(\mu_1)-1)(\beta_1(\mu_2)-\beta_1(\mu_1))(q_I^I)^{\beta_1(\mu_2)-\beta_1(\mu_1)-2} \\
&\times (q_I^A)^{-\beta_1(\mu_2)}\left(\frac{Kq_I^A-C}{\rho}\right) - q^{\beta_1(\mu_1)}(\beta_1(\mu_1)+1)\beta_1(\mu_1)(q_I^I)^{-\beta_1(\mu_1)-2}I \\
=&(q_I^I)^{-\beta_1(\mu_1)-2}\Bigg[q^{\beta_1(\mu_1)}(\beta_1(\mu_2)-\beta_1(\mu_1)-1)(\frac{q_I^I}{q_I^A})^{\beta_1(\mu_2)}(\beta_1(\mu_2)-\beta_1(\mu_1)) \\
&\times\left(\frac{Kq_I^A-C}{\rho}\right) - q^{\beta_1(\mu_1)}(\beta_1(\mu_1)+1)\beta_1(\mu_1)I\Bigg] \\
=&(q_I^I)^{-\beta_1(\mu_1)-2}\Bigg[q^{\beta_1(\mu_1)}(\beta_1(\mu_2)-\beta_1(\mu_1)-1)(\beta_1(\mu_2)-\beta_1(\mu_1)) \\
&\times\frac{\beta_1(\mu_1)I}{\beta_1(\mu_1)-\beta_1(\mu_2)} - q^{\beta_1(\mu_1)}(\beta_1(\mu_1)+1)\beta_1(\mu_1)I\Bigg] \\
=&-(q_I^I)^{-\beta_1(\mu_1)-2}\left[q^{\beta_1(\mu_1)}\beta_1(\mu_1)\beta_1(\mu_2)I\right] < 0. \qquad (5.53)
\end{aligned}$$

The second partial derivatives of $V^I(q)$ with respect to q_I^A is:

$$\begin{aligned}
\frac{\partial^2 V^I(q)}{(\partial q_I^A)^2} =& q^{\beta_1(\mu_1)}(q_I^I)^{\beta_1(\mu_2)-\beta_1(\mu_1)}\frac{K}{\rho}(1-\beta_1(\mu_2))(-\beta_1(\mu_2))(q_I^A)^{-\beta_1(\mu_2)-1} \\
&-(\beta_1(\mu_2)+1)\beta_1(\mu_2)q^{\beta_1(\mu_2)}(q_I^I)^{\beta_1(\mu_2)-\beta_1(\mu_2)}(q_I^A)^{-\beta_1(\mu_2)-2}\left(\frac{C}{\rho}\right) \\
=&q^{\beta_1(\mu_1)}(q_I^I)^{\beta_1(\mu_2)-\beta_1(\mu_1)}(q_I^A)^{-\beta_1(\mu_2)-2}\Bigg[\frac{K}{\rho}(\beta_1(\mu_2)-1)(\beta_1(\mu_2))q_I^A \\
&-(\beta_1(\mu_2)+1)\beta_1(\mu_2)\left(\frac{C}{\rho}\right)\Bigg] \\
=&-q^{\beta_1(\mu_1)}(q_I^I)^{\beta_1(\mu_2)-\beta_1(\mu_1)}(q_I^A)^{-\beta_1(\mu_2)-2}\beta_1(\mu_2)\left(\frac{C}{\rho}\right) < 0. \qquad (5.54)
\end{aligned}$$

The derivatives of $V^I(q)$ with respect to q_I^I and q_I^A is:

$$\begin{aligned}\frac{\partial^2 V^I(q)}{\partial q_I^I \partial q_I^A} =&(\beta_1(\mu_2)-\beta_1(\mu_1))(q_I^I)^{\beta_1(\mu_2)-\beta_1(\mu_1)-1}(q_I^A)^{-\beta_1(\mu_2)} \\ &\times\left[q^{\beta_1(\mu_1)}\frac{K}{\rho}(1-\beta_1(\mu_2))+\beta_1(\mu_2)q^{\beta_1(\mu_1)}\frac{1}{q_I^A}\left(\frac{C}{\rho}\right)\right] \\ =&(\beta_1(\mu_2)-\beta_1(\mu_1))(q_I^I)^{\beta_1(\mu_2)-\beta_1(\mu_1)-1}(q_I^A)^{-\beta_1(\mu_2)} \\ &\times\left[q^{\beta_1(\mu_1)}\frac{K}{\rho}(1-\beta_1(\mu_2))+\beta_1(\mu_2)q^{\beta_1(\mu_1)}\frac{\beta_1(\mu_2)-1}{\beta_1(\mu_2)}\frac{K}{\rho}\right] \\ =&0. \end{aligned} \tag{5.55}$$

Thus

$$D=\frac{\partial^2 V^I(q)}{(\partial q_I^I)^2}\frac{\partial^2 V^I(q)}{(\partial q_I^A)^2}-\left(\frac{\partial^2 V^I(q)}{\partial q_I^I \partial q_I^A}\right)^2>0. \tag{5.56}$$

Hence it is proved that the value of project run by the social planner $V^I(q)$ is maximized if the development phase starts at q_I^I and the quality standard is set to be q_I^A. ■

Proof of the Product of Two Non-Negative and Convex Functions is a Convex Function

In general, the product of two non-negative and convex functions is also a convex function. The proof is as follows:

Choose x and y in the domain with $x<y$ and t in [0,1] and consider the function

$$H(x)=f(x)g(x), \tag{5.57}$$

with both $f(x)$ and $g(x)$ non-negative and convex.

$$
\begin{aligned}
&H[tx+(1-t)y]-[tH(x)+(1-t)H(y)]\\
=&f[tx+(1-t)y]g[tx+(1-t)y]-[tf(x)g(x)+(1-t)f(y)g(y)]\\
\leq&[tf(x)+(1-tf(y))]\,[tg(x)+(1-t)g(y)]-[tf(x)g(x)+(1-t)f(y)g(y)]\\
\leq&t^2f(x)g(x)+t(1-t)f(x)g(y)+t(1-t)f(y)g(x)+(1-t)^2f(y)g(y)-tf(x)g(x)\\
&-(1-t)f(y)g(y)\\
\leq&tf(x)g(x)+(1-t)f(y)g(y)-tf(x)g(x)-(1-t)f(y)g(y)\\
=&0.
\end{aligned}
\tag{5.58}
$$

Hence $H[tx+(1-t)y] \leq [tH(x)+(1-t)H(y)]$ and it proves that $H(x)$ is a convex function.■

Proof of Proposition 5.7

Rewrite q_I^I by substituting q_I^A,

$$
\begin{aligned}
q_I^I &= q_I^A\left(\frac{\beta_1(\mu_1)I}{\beta_1(\mu_1)-\beta_1(\mu_2)}\frac{\rho}{Kq_I^A-C}\right)^{1/\beta_1(\mu_2)}\\
&= q_I^A\left(\frac{\beta_1(\mu_1)I}{\beta_1(\mu_1)-\beta_1(\mu_2)}\frac{\rho(\beta_1-1)}{C}\right)^{1/\beta_1(\mu_2)}\\
&= \frac{\beta_1(\mu_2)}{\beta_1(\mu_2)-1}\left(\frac{C}{K}\right)\left(\frac{\beta_1(\mu_1)I}{\beta_1(\mu_1)-\beta_1(\mu_2)}\frac{\rho(\beta_1-1)}{C}\right)^{1/\beta_1(\mu_2)}.
\end{aligned}
\tag{5.59}
$$

Then rewrite q_c^I by substituting q_c^A,

$$
\begin{aligned}
q_c^I &= q_c^A\left(\frac{\beta_1(\mu_1)}{\beta_1(\mu_1)-\beta_1(\mu_2)}\frac{\rho I}{R-C}\right)^{1/\beta_1(\mu_2)}\\
&= \frac{\beta_1(\mu_1)}{\beta_1(\mu_1)-1}\left(\frac{R}{K}\right)\left(\frac{\beta_1(\mu_1)}{\beta_1(\mu_1)-\beta_1(\mu_2)}\frac{\rho I}{R-C}\right)^{1/\beta_1(\mu_2)}.
\end{aligned}
\tag{5.60}
$$

Divide q_c^I by q_I^I,

$$W(C) = \frac{q_c^I}{q_I^I} = \frac{\beta_1(\mu_1)(\beta_1(\mu_2)-1)}{\beta_1(\mu_2)(\beta_1(\mu_1)-1)} \left(\frac{R}{C}\right) \left(\frac{C}{R-C}\frac{1}{\beta_1(\mu_2)-1}\right)^{1/\beta_1(\mu_2)}. \quad (5.61)$$

Take the first order derivative of $W(C)$ with respect to C,

$$\frac{\partial W(C)/\partial C}{A} = \left(-\frac{1}{C^2}\right)\left(\frac{C}{R-C}\right)^{1/\beta_1(\mu_2)} + \frac{1}{C}\frac{1}{\beta_1(\mu_2)}\left(\frac{C}{R-C}\right)^{1/\beta_1(\mu_2)-1}\frac{R}{(R-C)^2}, \quad (5.62)$$

where

$$A = \frac{\beta_1(\mu_1)(\beta_1(\mu_2)-1)}{\beta_1(\mu_2)(\beta_1(\mu_1)-1)} \left(\frac{1}{\beta_1(\mu_2)-1}\right)^{1/\beta_1(\mu_2)}. \quad (5.63)$$

And $\frac{\partial W(C)/\partial C}{A} = 0$ gives

$$C = \left(\frac{\beta_1(\mu_2)-1}{\beta_1(\mu_2)}\right) R. \quad (5.64)$$

The ratio $\frac{q_c^I}{q_I^I}$ can be treated as a function of C. Consider the two functions $f_1(C) = \frac{1}{C}$ and $f_2(C) = \left(\frac{C}{R-C}\right)^{1/\beta_1(\mu_2)}$. $f_1(C)$ is convex for every value of C. For computational convenience, denote $\alpha = 1/\beta_1(\mu_2)$ and

$$\begin{aligned}\frac{\partial^2 f_2(C)}{\partial^2 C} =& \frac{\partial^2 \left(\frac{C}{R-C}\right)^{\alpha}}{\partial^2 C} \\ =& R\alpha\left\{C^{\alpha-2}(R-C)^{-\alpha-2}\left[(\alpha-1)(R-C)+C((\alpha+1)\right]\right\} \\ =& R\alpha\left\{C^{\alpha-2}(R-C)^{-\alpha-2}\left[2C-(1-\alpha)R\right]\right\}. \end{aligned} \quad (5.65)$$

When $C = \left(\frac{\beta_1(\mu_2)-1}{\beta_1(\mu_2)}\right) R$,

$$\begin{aligned}
&\frac{\partial^2 f_2(C)}{\partial^2 C} \\
=&R\alpha\left\{C^{\alpha-2}(R-C)^{-\alpha-2}(1-\alpha)R\right\} \\
=&R\alpha\left\{C^{\alpha-2}(R-C)^{-\alpha-2}\left(\frac{\beta_1(\mu_2)-1}{\beta_1(\mu_2)}\right)R\right\} > 0.
\end{aligned} \tag{5.66}$$

Hence, the function $f_2(C)$ is convex on the point $C = \left(\frac{\beta_1(\mu_2)-1}{\beta_1(\mu_2)}\right) R$.

Since both functions $f_1(C)$ and $f_2(C)$ are non-negative and convex, the product of two non-negative and convex functions is also a convex function. See Appendix.

Because $W\left[\left(\frac{\beta_1(\mu_2)-1}{\beta_1(\mu_2)}\right)R\right] = \frac{\beta_1(\mu_1)}{\beta_1(\mu_1)-1} > 1$, the ratio $W(C) = \frac{q_c^I}{q_I^I}$ is larger than 1 when it takes the minimum value, which shows that $q_c^I > q_I^I$. ■

Proof of Proposition 5.8

If $q_c^A < q_I^A$, (see proposition 5.4 and equation 5.24), the following condition must be satisfied:

$$R < \frac{(\beta_1(\mu_1)-1)\beta_1(\mu_2)}{(\beta_1(\mu_2)-1)\beta_1(\mu_1)}C. \tag{5.67}$$

However, equation 5.28 will also be satisfied at the same time. Thus,

$$\frac{\beta_1(\mu_1)}{\beta_1(\mu_1)-\beta_1(\mu_2)}\rho I + C < R < \frac{(\beta_1(\mu_1)-1)\beta_1(\mu_2)}{(\beta_1(\mu_2)-1)\beta_1(\mu_1)}C. \tag{5.68}$$

Equation 5.68 only holds if the sunk cost of the project I satisfies,

$$\frac{\beta_1(\mu_1)}{\beta_1(\mu_1)-\beta_1(\mu_2)}\rho I + C < \frac{(\beta_1(\mu_1)-1)\beta_1(\mu_2)}{(\beta_1(\mu_2)-1)\beta_1(\mu_1)}C, \tag{5.69}$$

or

$$I < \frac{(\beta_1(\mu_1) - \beta_1(\mu_2))^2 C}{\beta_1(\mu_1)^2(\beta_1(\mu_2) - 1)\rho}. \tag{5.70}$$

Since it is by assumption that $q_c^I < q_c^A$ and it has been proved that $q_I^I < q_c^I$, $q_I^I < q_c^I < q_c^A < q_I^A$. ■

Proof of Proposition 5.9

If $q_I^A \leq q_c^A$, (see proposition 5.4 and equation 5.24), the following condition must be satisfied:

$$R \geq \frac{(\beta_1(\mu_1) - 1)\beta_1(\mu_2)}{(\beta_1(\mu_2) - 1)\beta_1(\mu_1)} C. \tag{5.71}$$

Since by assumption, $q_c^I \leq q_c^A$, the following condition holds

$$R > \frac{\beta_1(\mu_1)}{\beta_1(\mu_1) - \beta_1(\mu_2)} \rho I + C. \tag{5.72}$$

If

$$\frac{\beta_1(\mu_1)}{\beta_1(\mu_1) - \beta_1(\mu_2)} \rho I + C < \frac{(\beta_1(\mu_1) - 1)\beta_1(\mu_2)}{(\beta_1(\mu_2) - 1)\beta_1(\mu_1)} C, \tag{5.73}$$

the sunk cost I will be satisfying

$$I < \frac{(\beta_1(\mu_1) - \beta_1(\mu_2))^2 C}{\beta_1(\mu_1)^2(\beta_1(\mu_2) - 1)\rho}. \tag{5.74}$$

Hence

$$R \geq \frac{(\beta_1(\mu_1) - 1)\beta_1(\mu_2)}{(\beta_1(\mu_2) - 1)\beta_1(\mu_1)} C. \tag{5.75}$$

Next we prove that there is a unique R_c which makes $q_c^I = q_I^A$. Take the first order derivative of q_c^I with respect to R, we will find that $\frac{\partial q_c^I}{\partial R} < 0$ if $R \in \left[\frac{(\beta_1(\mu_1)-1)\beta_1(\mu_2)}{(\beta_1(\mu_2)-1)\beta_1(\mu_1)}C, \frac{\beta_1(\mu_2)}{\beta_1(\mu_2)-1}C\right)$ and $\frac{\partial q_c^I}{\partial R} \geq 0$ if $R \in \left[\frac{\beta_1(\mu_2)}{\beta_1(\mu_2)-1}C, \infty\right)$.

Moreover,

$$\frac{\beta_1(\mu_2)}{\beta_1(\mu_2)-1}C - \frac{(\beta_1(\mu_1)-1)\beta_1(\mu_2)}{(\beta_1(\mu_2)-1)\beta_1(\mu_1)}C = \frac{\beta_1(\mu_2)C}{(\beta_1(\mu_2)-1)\beta_1(\mu_1)} > 0. \tag{5.76}$$

When $R = \frac{(\beta_1(\mu_1)-1)\beta_1(\mu_2)}{(\beta_1(\mu_2)-1)\beta_1(\mu_1)}C$,

$$\begin{aligned} q_c^I &= \frac{\beta_1(\mu_2)}{\beta_1(\mu_2)-1}\frac{C}{K}\left[\frac{\beta_1(\mu_1)}{\beta_1(\mu_1)-\beta_1(\mu_2)}\frac{\rho I}{R-C}\right]^{1/\beta_1(\mu_2)} \\ &= q_I^A\left[\frac{\beta_1(\mu_1)}{\beta_1(\mu_1)-\beta_1(\mu_2)}\frac{\rho I}{R-C}\right]^{1/\beta_1(\mu_2)}. \end{aligned} \tag{5.77}$$

By assumption, $\left[\frac{\beta_1(\mu_1)}{\beta_1(\mu_1)-\beta_1(\mu_2)}\frac{\rho I}{R-C}\right]^{1/\beta_1(\mu_2)} < 1$, thus $q_c^I < q_I^A$.

Since

$$q_c^I = \frac{\beta_1(\mu_1)}{\beta_1(\mu_1)-1}\frac{R}{K}\left[\frac{\beta_1(\mu_1)}{\beta_1(\mu_1)-\beta_1(\mu_2)}\frac{\rho I}{R-C}\right]^{1/\beta_1(\mu_2)}, \tag{5.78}$$

to see what happen to q_c^I when R goes to infinity, we compute $\lim_{R\to+\infty}\frac{R}{(R-C)^{1/\beta_1(\mu_2)}}$ by using L'Hospital's Rule and $\lim_{R\to\infty}\frac{R}{(R-C)^{1/\beta_1(\mu_2)}} = \lim_{R\to\infty}\beta_1(\mu_2)(R-C)^{1-1/\beta_1(\mu_2)} = +\infty > q_I^A$. Thus there is a unique R_c makes $q_c^I = q_I^A$.

It is by assumption that $q_c^I < q_I^A$ and $q_I^I < q_c^I$. In conclusion, $q_I^I < q_c^I < q_I^A \leq q_c^A$ on $\left[\frac{(\beta_1(\mu_1)-1)\beta_1(\mu_2)}{(\beta_1(\mu_2)-1)\beta_1(\mu_1)}C, R_c\right)$ and $q_I^I < q_I^A \leq q_c^I < q_c^A$ on $\left[R_c, \infty\right)$.

If the Equation 5.73 is changed to be

$$\frac{\beta_1(\mu_1)}{\beta_1(\mu_1)-\beta_1(\mu_2)}\rho I + C \geq \frac{(\beta_1(\mu_1)-1)\beta_1(\mu_2)}{(\beta_1(\mu_2)-1)\beta_1(\mu_1)}C, \tag{5.79}$$

the sunk cost I will be satisfying

$$I \geq \frac{(\beta_1(\mu_1)-\beta_1(\mu_2))^2 C}{\beta_1(\mu_1)^2(\beta_1(\mu_2)-1)\rho}. \tag{5.80}$$

Hence

$$R \geq \frac{\beta_1(\mu_1)}{\beta_1(\mu_1)-\beta_1(\mu_2)}\rho I + C. \tag{5.81}$$

There are only two differences in the conclusion which is to change the start value to $R = \frac{\beta_1(\mu_1)}{\beta_1(\mu_1)-\beta_1(\mu_2)}\rho I + C$ and denote the critical value that makes $q_c^I = q_I^A$ as R_{cc}. The rest of the proofs are the same. The final conclusion will be $q_I^I < q_c^I < q_I^A \leq q_c^A$ on $\left[\frac{\beta_1(\mu_1)}{\beta_1(\mu_1)-\beta_1(\mu_2)}\rho I + C, R_{cc}\right)$ and $q_I^I < q_I^A \leq q_c^I < q_c^A$ on $\left[R_{cc}, \infty\right)$. ■

Proof of Proposition 5.11

Dependent on the initial value of product's quality q, the total value of the projects are different.

When $q < q_I^I < q_c^I$, the total value of both projects are:

$$V^S(q) + V^F(q) = \left(\frac{q}{q_c^I}\right)^{\beta_1(\mu_1)} \left[\left(\frac{q_c^I}{q_c^A}\right)^{\beta_1(\mu_2)} \left(\frac{Kq_c^A - C}{\rho}\right) - I\right] \tag{5.82}$$

and

$$V^I(q) = \left(\frac{q}{q_I^I}\right)^{\beta_1(\mu_1)} \left[\left(\frac{q_I^I}{q_I^A}\right)^{\beta_1(\mu_2)} \left(\frac{Kq_I^A - C}{\rho}\right) - I\right]. \tag{5.83}$$

q_I^I and q_c^I are the optimal investment thresholds of both projects and they solve the maximization problems of the social planner's project and the pharmaceutical company's project respectively. However, the maximization problem of the social planner's project is an unconstrained problem while the maximization problem of the pharmaceutical company's problem is limited by the quality standard set by

the government. In this case, the option value of the pharmaceutical company is not fully captured which leads to lower project value. Thus the total value of the decentralized project is lower than the social planner's project.

When $q_I^I < q_c^I < q$, both projects start immediately. The total value of both projects are:

$$V^S(q) + V^F(q) = \left(\frac{q}{q_c^A}\right)^{\beta_1(\mu_2)} \left(\frac{Kq_c^A - C}{\rho}\right) - I \tag{5.84}$$

and

$$V^I(q) = \left(\frac{q}{q_I^A}\right)^{\beta_1(\mu_2)} \left(\frac{Kq_I^A - C}{\rho}\right) - I. \tag{5.85}$$

In general, the total value of each project can be represented by the following function:

$$NPV(x) = \left(\frac{q}{x}\right)^{\beta_1(\mu_2)} \left(\frac{Kx - C}{\rho}\right) - I, \tag{5.86}$$

where $x > 0$.

Take the first order derivative of $NPV(x)$ wrt x,

$$NPV'(x) = q^{\beta_1(\mu_2)} x^{-\beta_1(\mu_2)-1} \left((1-\beta_1(\mu_2))\frac{Kx}{\rho} + \frac{C}{\rho}\beta_1(\mu_2)\right). \tag{5.87}$$

It is shown that $NPV'(x) > 0$ if $0 < x < \frac{\beta_1(\mu_2)}{\beta_1(\mu_2)-1}\frac{C}{K} = q_I^A$, $NPV'(x) = 0$ if $x = q_I^A$ and $NPV'(x) < 0$ if $x > q_I^A$.

Now take the second order derivative of $NPV(x)$ wrt x,

$$NPV''(x) = q^{\beta_1(\mu_2)}[-\beta_1(\mu_2)]x^{-\beta_1(\mu_2)-2}\left[(1-\beta_1(\mu_2))x\frac{K}{\rho} + \frac{C}{\rho}(\beta_1(\mu_2)+1)\right]. \tag{5.88}$$

It is shown that $NPV''(x) > 0$ if $x > \frac{\beta_1(\mu_2)+1}{\beta_1(\mu_2)-1}\frac{C}{K} = q_I^A + \frac{C}{(\beta_1(\mu_2)-1)K}$, $NPV'(x) = 0$ if $x = \frac{\beta_1(\mu_2)+1}{\beta_1(\mu_2)-1}\frac{C}{K}$ and $NPV'(x) < 0$ if $0 < x < \frac{\beta_1(\mu_2)+1}{\beta_1(\mu_2)-1}\frac{C}{K}$.

In conclusion, $NPV(x)$ is an increasing concave function on $(0, q_I^A)$ and reaches its maximum at q_I^A. Then it decreases and remains being concave on $(q_I^A, q_I^A + \frac{C}{(\beta_1(\mu_2)-1)K})$ then it keeps decreasing and being convex on $[q_I^A + \frac{C}{(\beta_1(\mu_2)-1)K}, \infty)$.

Thus,

$$\left(\frac{q}{q_I^A}\right)^{\beta_1(\mu_2)}\left(\frac{Kq_I^A - C}{\rho}\right) - I > \left(\frac{q}{q_c^A}\right)^{\beta_1(\mu_2)}\left(\frac{Kq_c^A - C}{\rho}\right) - I. \tag{5.89}$$

And it is proved that the value of the social planner's project is strictly larger than the decentralized project when $q_I^I < q_c^I < q$.

When $q_I^I < q < q_c^I$, the social planner's project starts immediately while the decentralized project has not started yet. The total value of both projects are:

$$V^S(q) + V^F(q) = \left(\frac{q}{q_c^I}\right)^{\beta_1(\mu_1)}\left[\left(\frac{q_c^I}{q_c^A}\right)^{\beta_1(\mu_2)}\left(\frac{Kq_c^A - C}{\rho}\right) - I\right] \tag{5.90}$$

and

$$V^I(q) = \left(\frac{q}{q_I^A}\right)^{\beta_1(\mu_2)}\left(\frac{Kq_I^A - C}{\rho}\right) - I. \tag{5.91}$$

Since the total value of the social planner's project is larger than the decentralized project when $q \in [0, q_I^I) \cup [q_c^I, +\infty]$, if $V^I(q)$ is more convex on $[q_I^I, q_c^I)$, $V^I(q) > V^S(q) + V^F(q)$.

Take the second order derivatives of Equation 5.91 with respect to q and

$$\begin{aligned}
\left[V^S(q)+V^F(q)\right]'' &= \left(\frac{q}{q_c^I}\right)^{\beta_1(\mu_1)}\left[\left(\frac{q_c^I}{q_c^A}\right)^{\beta_1(\mu_2)}\left(\frac{Kq_c^A-C}{\rho}\right)-I\right] \\
&\quad\times\beta_1(\mu_2)(\beta_1(\mu_2)-1)\frac{1}{q^2} \\
&< \left(\frac{q}{q_c^I}\right)^{\beta_1(\mu_2)}\left[\left(\frac{q_c^I}{q_c^A}\right)^{\beta_1(\mu_2)}\left(\frac{Kq_c^A-C}{\rho}\right)-I\right] \\
&\quad\times\beta_1(\mu_2)(\beta_1(\mu_2)-1)\frac{1}{q^2} \\
&< \left(\frac{q}{q_c^A}\right)^{\beta_1(\mu_2)}\left(\frac{Kq_c^A-C}{\rho}\right)\beta_1(\mu_2)(\beta_1(\mu_2)-1)\frac{1}{q^2} \\
&< \left(\frac{q}{q_I^A}\right)^{\beta_1(\mu_2)}\left(\frac{Kq_I^A-C}{\rho}\right)\beta_1(\mu_2)(\beta_1(\mu_2)-1)\frac{1}{q^2} \\
&= \left[V^I(q)\right]''. \qquad (5.92)
\end{aligned}$$

Hence we have proved that $V^I(q)$ is more convex on $[q_I^I, q_c^I)$. Thus the project value of the social planner's project is larger than the decentralized one. ■

Chapter 6

Gambling or Investment? A Time-Constrained Pharmaceutical Investment Decision under Uncertainty

6.1 Abstract

This chapter discusses whether a time-constrained pharmaceutical R&D project provides with more investment incentives to tackle the lack of investment problem on Neglected Tropical Diseases (NTDs). The success of the project is modeled by a Poisson process, which is assumed to be independent of the process of revenues. We claim that the intensity of the Poisson process plays an important role in the investment decisions if both time-to-expiration and the sudden success of the projects are considered simultaneously. The model shows that two effects determine the investment threshold of the time-constrained project: the investment effect and the gamble effect. The investment effect will reduce the optimal investment threshold while the gamble effect will increase it. Moreover the numerical results show that

the time-constrained project does provide with more investment incentives, when the life remaining of the project is longer, intensity of the Poisson process is higher and when uncertainty of revenues is lower.

6.2 Introduction

The problem to tackle the Neglected Tropical Diseases (NTDs) in developing countries has been long recognized. Trouiller et al. (2002) found that the infectious diseases present a huge burden expressed as millions of disability adjusted life-years (DALYs) in developing countries and together account for 11.4% of the global disease burden. However, only 1% of the 1393 new chemical entities marketed between 1975 and 1999 were registered for these diseases, in which 13 for Neglected Tropical Diseases (NTDs) and three for tuberculosis. The reason for the lack of investment problem is that the people who suffer from these diseases are mostly from developing countries with low income and they can not afford to pay for the drugs. Thus the pharmaceutical companies have no incentives to start these risky projects that subject to various technological and political uncertainties.

To address the lack of investment problem, the push and pull mechanisms proposed in the literature may serve to promote research into neglected infectious diseases (Mueller-Langer (2013)). Among all, the Advance Purchase Commitments (APC) is one of the best ways to increase investment incentives by assuring a future solid market. The Center for Global Development (CGD), with the support of the Bill & Melinda Gates Foundation published a report in 2005 recommending how advance market commitments for vaccines could be implemented Levine et al. (2005).

However, most of these commitments only specify specific technologies with certain quantities in the future at a guaranteed unit price (Farlow (2004)), without setting time constraints on the drug development process. In order words, the decision maker has an infinitely lived option to start the project. Moreover, the R&D process can last forever until some new product is developed once the project starts.

However, the assumption that the decision maker (DM) owns a perpetual investment option in the pharmaceutical industry seems too strong, since patients who are in serious medical conditions can not afford to wait forever. In this chapter, the thesis investigates how investment decisions are affected if a time constraint is added to the pharmaceutical R&D project.

Following Myers (1977), it is quite natural to think of many investment problems that feature irreversibility, flexibility and uncertainty as real options. Many pharmaceutical R&D projects can be fitted in this framework since they exhibit these features. Firstly, the cost spent on developing a drug is usually high and irreversible since it will not be recovered if the research turns out to be a failure or the project is abandoned in the meantime. Secondly, most of the decisions do not have to be made right away. Waiting while collecting useful information will usually help make a better decision. Lastly, the payoffs of projects are usually full of uncertainties in that the price and demand of drugs are usually not known ex ante. Because of these features, initiating the project at different time will lead to huge differences on the potential profits.

In the real options literature, there are many models that assume the investment decisions are allowed to be made within an unlimited time horizon. For instance, in the models that Schwartz and Moon (1996) and Hsu and Schwartz (2008) proposed to evaluate the pharmaceutical R&D projects, there are no time constraints for the investment decisions. The decision maker can wait forever until the condition is favorable enough before investment. However, in many practical cases, this is not realistic. In our models, we assume that the option of delaying investment does not live infinitely, but subject to a time constraint, say a T years time. This is similar to the real options models that are developed to evaluate the natural resource options, such as the valuation of a mine (Brennan and Schwartz (1985)) or the petroleum leases (Paddock et al. (1988)), where deadlines or time-to-expiration of the projects are also considered.

Another characteristic of the pharmaceutical R&D project is that the time that the project being successful is not know *ex ante*. For instance, the project may be

successful because of a major breakthrough of new technology. Such situation is usually modeled by using a Poisson process, with which the time between jumps follow exponential distribution. This is not new in the real options literature. For instance, the value of a project that exponentially decays or the project with sudden death can also be modeled by using this approach (Dixit and Pindyck (1994)).

The contribution of this chapter is that we provide with an evaluation method of a time-constrained pharmaceutical R&D project, of which success is modeled by using Poisson process. In other words, we consider a model with both time-to-expiration and sudden success of the project. Compared to other real options models to evaluate pharmaceutical R&D projects, such as Schwartz and Moon (1996), Hsu and Schwartz (2008) and Schwartz (2004), the model in this paper is different in two ways.

First, the intensity of the Poisson process, besides adding to the discount rate, also influences the timing of the investment decision by altering the success probability of the project, when time-to-expiration is considered. In Hsu and Schwartz (2008), the Poisson process is used to model catastrophic events when the decision maker is not limited by the time horizon. And it is argued that, if uncorrelated with the market, the intensity simply enters into the analysis through increasing the discount rates. We show that the intensity is more than simply adding to the discount rate.

Second, we model the sudden success of the project instead of the catastrophic events by using the Poisson process, which is different with the model of Schwartz (2004). In their paper, although time-to-expiration is also considered, the intensity simply adds to the discount rate since the catastrophic events do not have influence on the success probability of the project. In other words, intensity will have great impact on the investment decisions only if a) The success of the project is modeled by a Poisson process and b) When the project is of limited time horizon, are both satisfied simultaneously. Otherwise, the intensity is a less important parameter which does not have decisive effects on the investment decisions.

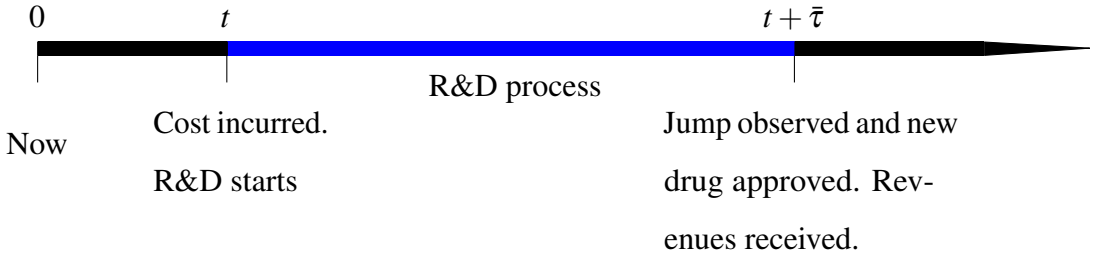
In this chapter, pharmaceutical R&D projects with and without time constraints are compared and there are three main findings. First, when the success of a time-constrained pharmaceutical R&D project is modeled by the Poisson process, the investment effect and the gamble effect determines the optimal investment thresholds of the project at any given time as the life remaining of the project decreases. The investment effect will reduce the optimal investment threshold while the gamble effect will increase it. Second, the intensity of the Poisson process will only have influence on the investment effect while the uncertainty of the project will only have impact on the gamble effect. Moreover, both effects increase as the project approaches the deadline. Last, the time-constrained project provides with more investment incentives, when intensity is higher and when uncertainty is lower.

The remainder of the chapter is organized as follow. Section 6.3 introduces the project with perpetual investment option. Section 6.4 discusses the time-constrained project. In section 6.5, the comparative statics of the two projects are shown. Section 6.6 considers policy implications. Finally, section 6.7 concludes the chapter.

6.3 The Project with a Perpetual Investment Option

The following model and results in this section are not new in the real options literature. They serve as benchmarks in order to compare with the model and results in section 6.4.

The time line of the project is as follows:



Consider a pharmaceutical company that has an opportunity to invest in a R&D project without a deadline. The investment is irreversible and subject to a sunk cost

$I > 0$ that is paid at the start of the project and a stream of cost flows $C > 0$ paid for every period of the R&D process. An advance purchase commitments (APC) contract is signed between the government and the pharmaceutical company, stating that the government promises to purchase a certain quantity of the products from the company, if the final product is proved to be successful anytime after investment. The revenues of the company are uncertain and represented by a stochastic process $(Y_t)_{t\geq 0}$, which follows a geometric Brownian motion (GBM)

$$dY_t = \mu Y_t dt + \sigma Y_t dB_t, \tag{6.1}$$

where $(B_t)_{t\geq 0}$ is a Wiener process, μ and σ are constants, and $Y_0 = y$.

The R&D process is modeled as a Poisson process $(q_t)_{t\geq 0}$, with intensity λ, and independent of $(B_t)_{t\geq 0}$. We assume that the process starts when the investment takes place and the start value is $q_0 = 0$. The final product is considered to be successful when the first jump is observed after investment, i.e., at the stopping time

$$\bar{\tau} = \inf\{t \geq 0 | q_t = 1\}. \tag{6.2}$$

It is assumed that the pharmaceutical company is risk neutral which discounts projects at rate $\rho > max\{0, \mu\}$. When the drug is successful, the company will be receiving a stream of revenues, of which the value is dependent on the value of Y_t at that time:

$$\begin{aligned} F(Y_t) &= E_{Y_t}\left(\int_t^\infty e^{-\rho(s-t)} Y_s ds\right) \\ &= \frac{Y_t}{\rho - \mu}. \end{aligned} \tag{6.3}$$

At the time of investment, the net present value (NPV) of the project is composed of three parts: (1) the sunk cost paid immediately; (2) the sum of the discounted cost flows during the R&D process and (3) the revenues received afterwards when

the final product is successful. The NPV of the project at time t is:

$$G(Y_t) = E_{Y_t}\left[\left(\int_t^{t+\bar{\tau}} e^{-\rho(s-t)}(-C)ds + \int_{t+\bar{\tau}}^{\infty} e^{-\rho(s-t)}Y_s ds - I\right)\right]. \tag{6.4}$$

Proposition 6.1 *If the investment takes place at anytime t, the NPV of the project at time t is*

$$G(Y_t) = \frac{\lambda Y_t}{(\rho-\mu)(\rho+\lambda-\mu)} - \left(\frac{C}{\rho+\lambda} + I\right). \tag{6.5}$$

See proof of Proposition 6.1 in the Appendix.

The pharmaceutical company wants to maximize the value of the project which is denoted by the following optimal stopping problem:

$$\begin{aligned} F^*(y) &= \sup_{\tau} E_y\left[-\int_{\tau}^{\tau+\bar{\tau}} e^{-\rho t}C dt + \int_{\tau+\bar{\tau}}^{\infty} e^{-\rho t}Y_t dt - e^{-\rho\tau}I\right] \\ &= \sup_{\tau} E_y\left\{e^{-\rho\tau}E_{Y_\tau}\left[-\int_0^{\bar{\tau}} e^{-\rho t}C dt + \int_{\bar{\tau}}^{\infty} e^{-\rho t}Y_t dt - I\right]\right\} \\ &= \sup_{\tau} E_y\left\{e^{-\rho\tau}\left[\frac{\lambda Y_\tau}{(\rho-\mu)(\rho+\lambda-\mu)} - \left(\frac{C}{\rho+\lambda}+I\right)\right]\right\} \\ &= \sup_{\tau} E_y\left[e^{-\rho\tau}G(Y_\tau)\right] \end{aligned} \tag{6.6}$$

The stopping time of which the investment in R&D becomes optimal is denoted by τ. As in most of the real options literature, the optimal stopping time takes the form of the first hitting times of some threshold Y^*. For $Y^* > 0$, denote the first passage time of Y^* by $\tau(Y^*) := \inf\{t \geq 0 \mid Y_t \geq Y^*\}$, which is the optimal time of investment. Therefore, the problem can be written as

$$\begin{aligned} F^*(y) &= \sup_{Y^*} E_y\left[e^{-\rho\tau(Y^*)}G(Y_{\tau(Y^*)})\right] \\ &= \sup_{Y^*} E_y\left[e^{-\rho\tau(Y^*)}\right]G(Y^*). \end{aligned} \tag{6.7}$$

In addition, the space $[0,\infty]$ can be divided into two regions by the critical value Y^* in this problem. In $[0,Y^*)$, continuation (waiting) is optimal since the value of investing immediately is less than the value of waiting. In $[Y^*,\infty]$, termination (invest immediately) is optimal since the value of investing immediately is equal to the value of waiting. Hence $[0,Y^*)$ is the continuation region while $[Y^*,\infty]$ is the stopping region (Dixit and Pindyck (1994)).

The characteristic operator of the process $(Y_t)_{t\geq 0}$, as we have seen before, is

$$\mathscr{L}_Y = \frac{1}{2}\sigma^2 y^2 \frac{\partial^2}{\partial y^2} + \mu y \frac{\partial}{\partial y}. \tag{6.8}$$

On the continuation region, the Bellman equation should hold, i.e., $\mathscr{L}_Y F^* = \rho F^*$. By substituting the expression of the characteristic operator and rearranging, we have

$$\frac{1}{2}\sigma^2 y^2 \frac{\partial^2 F^*}{\partial y^2} + \mu y \frac{\partial F^*}{\partial y} - \rho F^* = 0, \tag{6.9}$$

the general solution of which is of the form,

$$\varphi(y) = Ay^{\beta_1} + By^{\beta_2}, \tag{6.10}$$

where $\beta_1 > 1$ and $\beta_2 < 0$ are the two roots of the quadratic equation,

$$\mathscr{Q}(\beta) = \frac{1}{2}\sigma^2 \beta(\beta-1) + \mu\beta - \rho = 0. \tag{6.11}$$

The boundary condition $\varphi(0) = 0$ is satisfied only if $B = 0$, so that $\varphi(y) = Ay^{\beta_1}$ on $[0,Y^*)$. By using Dynkin's formula, the expected discount factor is

$$E_y\left[e^{-\rho\tau(Y^*)}\right] = \frac{\varphi(y)}{\varphi(Y^*)} = \left(\frac{y}{Y^*}\right)^{\beta_1}, \tag{6.12}$$

so that Y^* can be obtained by solving

$$\varphi(Y^*)G'(Y^*) = \varphi'(Y^*)G(Y^*). \tag{6.13}$$

which yields

$$Y^* = \frac{\beta_1}{\beta_1 - 1} \frac{(\rho - \mu)(\rho + \lambda - \mu)}{\lambda} \left(\frac{C}{\rho + \lambda} + I \right). \tag{6.14}$$

Therefore the value of the project is:

$$F^*(y) = \begin{cases} \left(\frac{y}{Y^*}\right)^{\beta_1} \left[\frac{\lambda Y^*}{(\rho-\mu)(\rho+\lambda-\mu)} - \left(\frac{C}{\rho+\lambda} + I \right) \right] & if \quad y < Y^* \\ \frac{\lambda y}{(\rho-\mu)(\rho+\lambda-\mu)} - \left(\frac{C}{\rho+\lambda} + I \right) & if \quad y \geq Y^*. \end{cases} \tag{6.15}$$

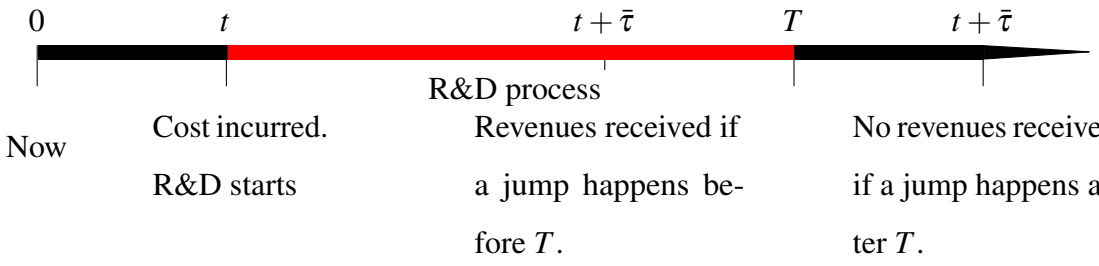
The project value of the perpetual option depends on the current value y of the stochastic process $(Y_t)_{t \geq 0}$. If the current value y is less than the optimal investment threshold Y^*, the optimal strategy of the pharmaceutical company is to wait and invest when Y^* is reached. However, if the current value y is larger or equal to the optimal investment threshold Y^*, the optimal strategy is to invest or start the R&D process right away.

6.4 The Time-Constrained Project

Now consider the case that another requirement is added in the previous advance purchase commitments contract, which states that the final product needs to be finished in T years time. After T years from now, the government will no longer guarantee to purchase the product from the pharmaceutical company even if any product is invented. Since the R&D process is modeled by a Poisson process, if a jump happens within the time specified by the government, i.e., T years, the project is considered to be successful and the pharmaceutical company will be rewarded. However, if no jump is observed within time T, the project will keep incurring

costs until time T and fails without receiving any revenues. Moreover, there is no opportunity to resume research or restart the project from the scratch. In this case, the value of the project does not only depend on the value of $(Y_t)_{t\geq 0}$, but also on time itself.

The time line of the project is as follows:



According to whether the jump happens by the time T, the NPV of the project can be separated into two parts. One part is the revenues of the project net of all the costs occurred before the jump happens, multiplied by the probability that the jump happens. The other part is the sum of all the costs accumulated by time T, multiplied by the probability that the jump does not happen, and no revenues are generated in this case.

The NPV of the project that at time t if $t < T$ is

$$\begin{aligned} g(Y_t,t) =& E_{Y_t}\left[\left(\int_t^{t+\bar{\tau}} e^{-\rho(s-t)}(-C)ds + \int_{t+\bar{\tau}}^{\infty} e^{-\rho(s-t)}Y_s ds - I\right) P(\bar{\tau} < T-t)\right. \\ &\left. + \left(\int_t^{T} e^{-\rho(s-t)}(-C)ds - I\right) P(\bar{\tau} \geq T-t)\right]. \end{aligned} \tag{6.16}$$

Proposition 6.2 *The NPV of the project is* 0 *if the investment takes place after time* T. *For any time* $t < T$ *at which the investment takes place, the NPV of the project is*

$$\begin{aligned} g(Y_t,t) =& \left[\frac{\lambda Y_t}{(\rho-\mu)(\rho+\lambda-\mu)} - \left(\frac{C}{\rho+\lambda} + I\right)\right]\left[1 - e^{-\lambda(T-t)}\right] \\ &+ \left[\frac{C\left(e^{-\rho(T-t)}-1\right)}{\rho} - I\right] e^{-\lambda(T-t)}. \end{aligned} \tag{6.17}$$

See proof of Proposition 6.2 in the Appendix.

The problem of the pharmaceutical company is to maximize the value of the project, which is denoted by the following optimal stopping problem

$$\begin{aligned}
F^*(y,t) &= \sup_{\tau\le T} E_y\left[\left(\int_\tau^{\tau+\bar\tau} e^{-\rho s}(-C)ds + \int_{\tau+\bar\tau}^{\infty} e^{-\rho s}Y_s ds - e^{-\rho\tau}I\right)P(\bar\tau < T-\tau)\right. \\
&\qquad \left. + \left(\int_\tau^{T} e^{-\rho s}(-C)ds - e^{-\rho\tau}I\right)P(\bar\tau \ge T-\tau)\right] \\
&= \sup_{\tau\le T} E_y\left\{e^{-\rho\tau}E_{Y_\tau}\left[\left(-\int_0^{\bar\tau} e^{-\rho s}Cds + \int_{\bar\tau}^{\infty} e^{-\rho s}Y_t ds - I\right)\right.\right. \\
&\qquad \left.\left. \times P(\bar\tau < T-\tau) + \left(\int_0^{T-\tau} e^{-\rho s}(-C)ds - I\right)P(\bar\tau \ge T-\tau)\right]\right\} \\
&= \sup_{\tau\le T} E_y\left\{e^{-\rho\tau}\left[\left[\frac{\lambda Y_\tau}{(\rho-\mu)(\rho+\lambda-\mu)} - \left(\frac{C}{\rho+\lambda}+I\right)\right]\left[1-e^{-\lambda(T-\tau)}\right]\right.\right. \\
&\qquad \left.\left. + \left[\frac{C\left(e^{-\rho(T-\tau)}-1\right)}{\rho} - I\right]e^{-\lambda(T-\tau)}\right]\right\} \\
&= \sup_{\tau\le T} E_y\left[e^{-\rho\tau}g(Y_\tau,\tau)\right]. \qquad (6.18)
\end{aligned}$$

Since the project value is influenced by both $(Y_t)_{t\ge 0}$ and t, the continuation region in this project is different from the one in the project of perpetual option. We define the continuation region as $\mathscr{C} = \{(Y_t,t) : Y_t \in [0, Y^*(t)\}$, for $t < T$, where waiting is the best strategy for the given contract length. And the stopping region is define as $\mathscr{S} = \{(Y_t,t) : Y_t \in [Y^*(t),\infty)\}$, for $t < T$, where the optimal strategy is to invest immediately.

On the continuation region, the Bellman equation should hold

$$\frac{\partial F^*}{\partial t} + \frac{1}{2}\sigma^2 y^2 \frac{\partial^2 F^*}{\partial y^2} + \mu y \frac{\partial F^*}{\partial y} - \rho F^* = 0. \qquad (6.19)$$

Because two state variables are involved in the time-constrained project, the differential equations that emerge from dynamic programming are also partial differential equations (PDE) with two state variables. And there is no general solution for the PDE. Hence we are not able to compute the closed form of the

expected discount factor by using Dynkin's formula as in the previous case. Solution of such equations typically requires numerical methods (see Dixit and Pindyck (1994)). In what follows, we try to solve the above PDE numerically by using the finite difference approximation.

To simplify the approximation, we first take the log transformation of the Bellman equation and define

$$x = \log(y) \tag{6.20}$$

$$W(x,t) = F^*(y,t) \tag{6.21}$$

$$w(x,t) = g(x,t). \tag{6.22}$$

Thus we can rewrite the partial differences in equation 6.19 as

$$\frac{\partial F^*}{\partial y} = \frac{\partial W}{\partial x} e^{-x} \tag{6.23}$$

$$\frac{\partial^2 F^*}{\partial y^2} = (\frac{\partial^2 W}{\partial x^2} - \frac{\partial W}{\partial x}) e^{-2x} \tag{6.24}$$

$$\frac{\partial F^*}{\partial t} = \frac{\partial W}{\partial t}. \tag{6.25}$$

Substitute equation 6.19 with equations 6.23 to 6.25, the transformed Bellman equation becomes

$$\frac{\partial W}{\partial t} + \frac{1}{2}\sigma^2 \frac{\partial^2 W}{\partial x^2} + (\mu - \frac{1}{2}\sigma^2)\frac{\partial W}{\partial x} - \rho W = 0. \tag{6.26}$$

The finite difference method transforms the continuous state variables Y_t and T into discrete variables and replaces the partial derivatives in the PDE with finite differences.

Let $W(x,t) \equiv W(i\triangle x, j\triangle t) \equiv W_{i,j}$, where $0 \leq i \leq k$ and $0 \leq j \leq h$. For any value of x, it is divided into i shares of equal lengths, which is represented by $\triangle x$ and hence $x = i\triangle x$. Similarly, for any value of t, it is divided into j shares of equal lengths, represented by $\triangle t$ and $x = j\triangle t$. Note that i and j do not have to be equal.

In addition, The partial differences in equation 6.26 can be approximated by

$$\frac{\partial^2 W}{\partial x^2} \approx [W_{i+1,j} - 2W_{i,j} + W_{i-1,j}]/(\triangle x)^2 \tag{6.27}$$

$$\frac{\partial W}{\partial x} \approx [W_{i+1,j} - W_{i-1,j}]/2\triangle x \tag{6.28}$$

$$\frac{\partial W}{\partial t} \approx [W_{i,j} - W_{i,j-1}]/\triangle t. \tag{6.29}$$

Now substitute equation 6.26 with equations 6.27 to 6.29,

$$\frac{(W_{i,j} - W_{i,j-1})}{\triangle t} + \frac{1}{2}\sigma^2 \frac{(W_{i+1,j} - 2W_{i,j} + W_{i-1,j})}{(\triangle x)^2} + (\mu - \frac{1}{2}\sigma^2)\frac{(W_{i+1,j} - W_{i-1,j})}{2\triangle x} - \rho W_{i,j} = 0. \tag{6.30}$$

The partial differential equation then can be written as

$$(1 + \rho\triangle t)W_{i,j-1} = p^+ W_{i+1,j} + p^0 W_{i,j} + p^- W_{i-1,j} \tag{6.31}$$

where

$$p^+ = \left[\frac{1}{2}\left(\frac{\sigma}{\triangle x}\right)^2 + \frac{1}{2}\left(\frac{\mu - \frac{1}{2}\sigma^2}{\triangle x}\right)\right]\triangle t \tag{6.32}$$

$$p^0 = 1 - \left(\frac{\sigma}{\triangle x}\right)^2 \triangle t \tag{6.33}$$

$$p^- = \left[\frac{1}{2}\left(\frac{\sigma}{\triangle x}\right)^2 - \frac{1}{2}\left(\frac{\mu - \frac{1}{2}\sigma^2}{\triangle x}\right)\right]\triangle t. \tag{6.34}$$

Notice that $p^+ + p^0 + p^- = 1$, thus they can be considered as the probabilities that the value of the W_i at time $j-1$, multiplied by some discount factor $1 + \rho\triangle t$, move upward p^+, not changed p^0 or move downwards p^-, in the next period j. More specifically, it is a three-point random walk representation of the Geometric Brownian Motion (GBM).

There are several boundary conditions that need to be satisfied. Firstly, no matter what value x is, at deadline T, the project value $F^*(y,T)$ is 0 since the opportunity

has been lost according to the requirement of the government. Hence

$$W(x,T) = 0; \text{(terminal boundary condition)}. \tag{6.35}$$

Secondly, if the initial value $y = 0$, the project value is also zero. According to the properties of GBM, the stochastic process $(Y_t)_{t\geq 0}$ will remain to be 0 in expectation since $E(Y_t) = ye^{\mu t}$. So, if $y = 0$, $E(Y_t) = 0$. When y approaches 0 from the right, i.e., $y \to 0^+$, x approaches $-\infty$, thus

$$W(-\infty,t) = 0; \text{(lower boundary condition)}. \tag{6.36}$$

As for the upper boundary condition, the value of x is chosen to be high enough so that there is at least one positive NPV of the project ($w(x,t) > 0$) to start with from time $T - \triangle t$.

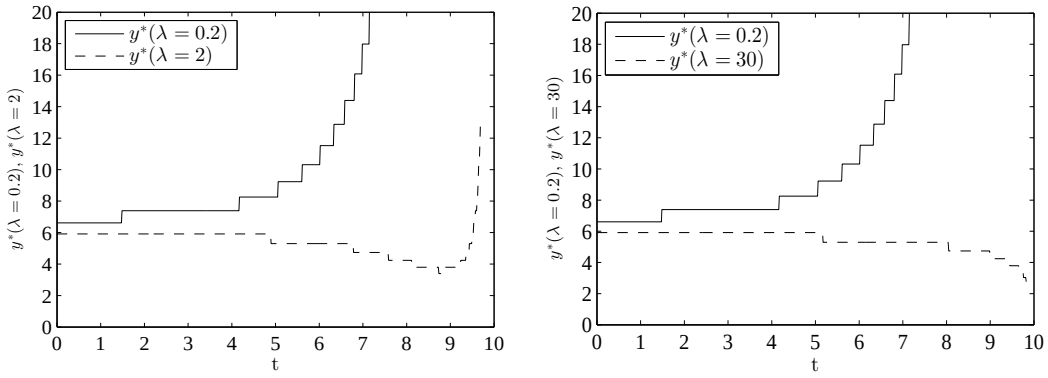
Next, we are going to find the boundary that separates the continuation region and the stopping region in log terms, namely the curve $x^*(t)$ which is called a "free boundary" (Dixit and Pindyck (1994)). We start from the terminal boundary and look backwards to find the first column that has at least one positive NPV by investing immediately. In that column, the value of the project equals the NPV of the project which can be computed by the equation in Proposition 6.1 since the NPVs one period after this column are all negative. Then we start to look at all the columns earlier by comparing the NPVs with the value of waiting in every grids of the trinomial trees. The smallest x that makes the value of waiting larger than NPV in each column is denoted by $x^*(t)$ which are the optimal investment thresholds at that time. The continuation region for a given t is composed of all the x that is less than $x^*(t)$ and all the x that is larger than $x^*(t)$ forms the stopping region. The collection of $x^*(t)$ in every column forms the optimal investment threshold frontier.

Proposition 6.3 *If the function after transformation $W(x,t)$ is maximized at $x = x^*(t)$, the original function $F^*(y,t)$ is maximized at $y = y^*(t)$.*

See proof of Proposition 6.3 in the Appendix.

6.5 Comparative Statics

The first problem that we discuss is how the investment threshold of the project that has limited life time changes, as the life of the project t approaches the time limit T under different intensity λ, which is shown in Figure 6.1. Generally speaking, the changes of the investment threshold result from the interaction of two effects, the investment effect and the gamble effect.



(A) λ=0.2 & 2 (B) λ=2 & 30

Fig. 6.1 The investment threshold of the time-constrained project varies with the project's life time t, when the intensity λ are 0.2, 2 and 30. The parameter values are: $\rho = 0.1$, $\mu = 0.08$, $C = 2$, $I = 50$, $\sigma = 0.5$ and $T = 10$

The investment effect is that the decreasing life remaining of the project, $T - t$, encourages earlier investment. As the remaining life of the project decreases, the project is less likely to be successful since there is less time for R&D. Hence the probability of the jump happening within the remaining life time of the project is low. In this case, a reasonable strategy would be to start the project sooner so that there will be more time for R&D, which increases the probability that the jump will happen within the time limit. Thus the investment effect will lead to a lower investment threshold.

On the contrary, the gamble effect is that the decreasing life remaining of the project delays investment. When it is close to the deadline, the probability that the jump will happen in time is low and the risk of starting the project is high. While the best strategy that the decision makers will make at this point is probably to

reject the investment proposal, the only possibility that the investment will take place is that the potential revenues are extremely high once the project is successful. Since the revenues of the project are positive related with the underlying stochastic process Y_t, the investment will take place only if Y_t is extremely high. Because the probability that the investment takes place when Y_t is of an extremely high value is low, the success of the project will be dependent on the event of small probabilities, which is similar to gambling. That is why we call it the gamble effect, which delays investment.

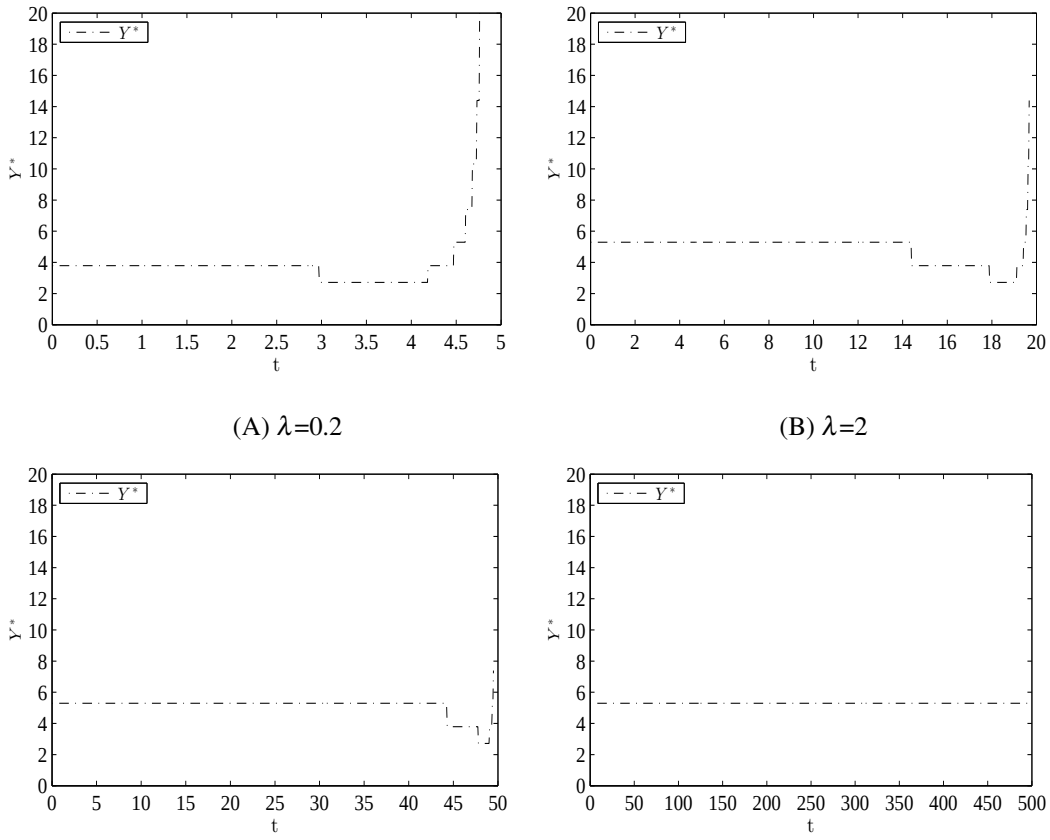
When $\lambda = 0.2$, it is shown that the investment threshold goes up as the life of project gets closer to the time limit T. The intensity λ represents the average number of jumps that happen within a unit time, a lower λ implies that the happening of the jump is lower. The investment effect is weaker for a lower λ, since even if the project starts sooner which means a longer possible R&D process, the chances that the jump will happen is still low. Thus the extension of the R&D process is less valuable than if the intensity is higher. In this case, the gamble effect dominates throughout the lifetime of the project, and the optimal investment threshold of the project keeps rising as the project approaches the deadline.

When $\lambda = 2$, it is shown that the investment threshold first goes down, then goes up by the end of the contract, and it eventually disappears before the deadline as the project approaches the deadline T. When intensity is higher, the chance that the jump happens is also higher. Thus the investment effect is stronger since earlier investment and a longer R&D process is more beneficial if the jump is more likely to happen. In this case, the risk of the project is lower, and the decision maker does not necessarily need to wait and start the project only if Y_t is extremely high. It is before y^* reaches its minimum that the investment effect dominates.

However, the two effects are reversed before the deadline. Because even if the intensity is higher, when it is close to the deadline, the time for the R&D process is too short for the jump to happen. This is when the gamble effect gets stronger and finally dominates the investment effect before the deadline of the project. Finally, as t further approaches T, the optimal investment threshold no longer exists. From this

point onwards, it is never optimal to accept the investment proposal since the NPVs of the project are all negative.

When λ further increases to $\lambda = 30$, the investment effect is so strong that the investment threshold of the project keeps decreasing even when the project is extremely close to the deadline. The gamble effect never dominates in this circumstance. It is worth noting that both effects are getting stronger as the life remaining of the project is decreasing. In addition, λ only has influence on the investment effect while the gamble effect is not affected when λ varies.



(A) λ=0.2 (B) λ=2

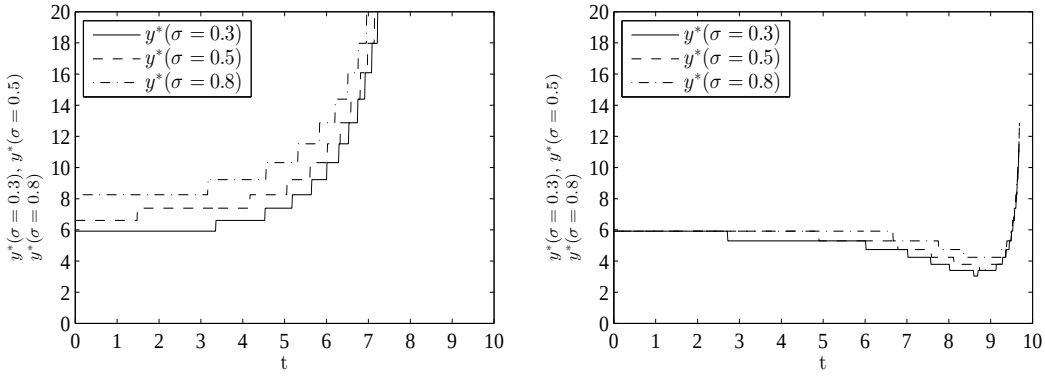
(A) λ=0.2 (B) λ=2

Fig. 6.2 The investment threshold of the time-constrained project varies with the project's life time t when the deadline of the project varies from 5 to 500 years. The parameter values are: $\rho = 0.1$, $\mu = 0.08$, $\sigma = 0.3$, $C = 2$ and $I = 50$.

Next, in Figure 6.2, we discuss how the investment threshold of the project that has time-constraint varies as the contract length increases. Summarily, as T

increases, the time-constraint will have less effect on the investment decision. More specifically, when T is great enough or goes to infinity, the time-constrained project becomes more similar to the unconstrained project and the investment threshold approaches a constant . The reason is, when T is large enough, the probability that the jump happens within the time limit, i.e., $P(\bar{\tau} < T - t)$, is 1, which makes the NPV function of the time-constrained project (see equation 6.16) becomes that of the unconstrained project (see equation 6.5).

Moreover, the shape of the free boundary is not general. In other models where time constraints are considered, as the project approaches the deadline, the investment threshold keeps decreasing if there exists only the investment effect with which the success probability of the project can only be enhanced by earlier investment. In this model, as it is closed to the deadline, it is the balance of both the investment and gamble effect determines the shape of the threshold. Since it is possible that the gamble effect is stronger, the investment threshold may increase as "t" approaches "T".



(A) λ=0.2 (B) λ=2

Fig. 6.3 The investment threshold of the time-constrained project varies with the project's life time t when uncertainty σ are 0.3, 0.5 and 0.8 respectively. The parameter values are: $\rho = 0.1$, $\mu = 0.08$, $C = 2$, $I = 50$ and $T = 10$.

Next, in Figures 6.3, this thesis discusses the effect of uncertainty σ has on the investment threshold of the project at different time t when intensity takes the value of $\lambda = 0.2$ and $\lambda = 2$, respectively.

Figure 6.3 (A) shows that the investment threshold of the time-constrained project increases as σ goes up for any given time t. This is standard in the real options literature (see Dixit and Pindyck (1994)) since the option value increases with uncertainty while the NPV of the project is not affected, which leads to the increase of the investment threshold. As t changes, the effect that uncertainty σ has on the option values forms the gamble effect. In other words, the increase in the level of uncertainty will boost the magnitude of the gamble effect. However, as it is shown in the figure, the gap between the threshold with different σ shrinks as t approaches T. The reason is that the gamble effect does not only dependent on the level of uncertainty σ, but also dependent on the time left of the project $T-t$. As the project approaches its deadline or when $T-t$ is smaller, as σ goes up, the gamble effect increases slower because waiting becomes more risky in the sense that there is less time left for the jump to happen. Thus, although the investment threshold increases as σ goes up for every time t, as it is close to the deadline, the increase of σ will have less effect on the gamble effect, which leads to the smaller gap between the investment threshold for different σ.

In Figure 6.3 (B), when the project is away from the deadline T, it is shown that the investment threshold does not change as σ goes up. This is because the investment effect dominates when λ is high. Thus even if an increase in σ boost up the gamble effect, the investment threshold does not go up. As t goes up, the investment threshold of the project that has lower uncertainty goes down first while the one with higher uncertainty stays the same. Since the gamble effect is stronger with higher uncertainty which offsets the investment effect, the investment thresholds when $\sigma = 0.5$ and $\sigma = 0.8$ decrease more slowly. However, since the intensity λ is not high enough, at a certain time t near the deadline, the two effects are reversed.

It is worth noting that the level of uncertainty σ has nothing to do with the investment effect but it is positive related with the gamble effect.

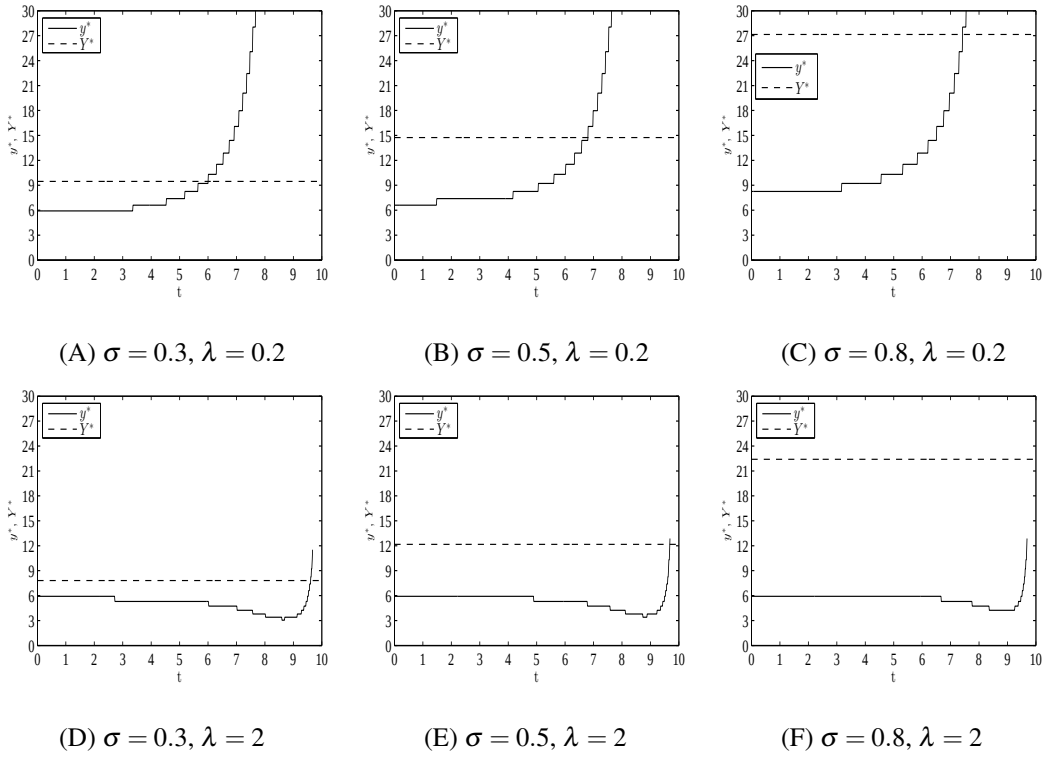
The investment problem of the project that has time constraint is quite similar to the exercise problem of the standard American call option. However, there are some differences between the two.

On one hand, as it is close to the deadline, the line of NPV=0 for the project goes up while it goes down for the American call option. For the project that has time constraint, when the time of the project approaches the maximum length of the contract "T", the probability that the project to be successful becomes lower and the total costs paid will be much higher. In this case, a positive NPV of project requires that revenues of the project must be higher, which leads to the increasing line when NPV=0. For the American call option, the NPV of the option at each point in time is dependent on three factors, which are the price of the underlying asset (P_t), the strike price (K) and the price of the call option (C_t) itself. The NPV of the option, $NPV(P_t) = max(P_t - K - C_t, 0)$. As the time approaches the deadline, the price of option decreases, thus the line that NPV=0 also decreases.

On the other hand, for the American call option, it is never optimal to exercise before the expiration date if there are no dividends. However, for the project that has time constraint, the decision maker should exercise the option or invest immediately when the NPV of the project is larger than the option value of the project.

Lastly, we discuss the difference of the project with a perpetual option with the time-constrained project by looking at how investment thresholds of both projects vary under different intensity λ and level of uncertainty σ.

It is shown in Figure 6.4 that the investment threshold of the project with a perpetual option does not vary with time t. In other words, the investment threshold is not a time-dependent function. Since for the project with a perpetual option, the life time remaining is infinity. Thus the decision maker can wait as long as he likes and the project will only end if the opportunity is given up or the decision maker decides to wait forever. If there is no time limit on waiting, the option value can be fully captured since the project will only start when Y_t is high enough. However, in the time-constrained project, the life remaining of the project has to be considered since the project fails automatically if the investment is not taken place within the time limit. The option value of this type of project can not be fully captured. In a word, the two projects' different capabilities of capturing the option values lead to the great difference of the two investment thresholds.



(A) $\sigma = 0.3$, $\lambda = 0.2$ (B) $\sigma = 0.5$, $\lambda = 0.2$ (C) $\sigma = 0.8$, $\lambda = 0.2$

(D) $\sigma = 0.3$, $\lambda = 2$ (E) $\sigma = 0.5$, $\lambda = 2$ (F) $\sigma = 0.8$, $\lambda = 2$

Fig. 6.4 Comparison of the investment thresholds of the perpetual option project Y^*, with the time-constrained project y^* when λ takes the value of $\lambda = 0.2$ and $\lambda = 2$, the level of uncertainty $\sigma = 0.3$, $\sigma = 0.5$ and $\sigma = 0.8$. The other parameter values are: $\rho = 0.1$, $\mu = 0.08$, $C = 2$, $I = 50$ and $T = 10$.

When λ is small, the investment threshold of the project with a perpetual option is larger than the one of the time-constrained project with long time remaining $T - t$. As the life-remaining of the project decreases, the investment threshold of the time-constrained project y^*, goes up and it exceeds the investment threshold of the project with a perpetual option Y^* at certain time t. As σ goes up, the option value increases and the time that $y^* \geq Y^*$ happens later. This is due to the two projects' different capabilities of capturing the option values. Thus at any time t, as σ goes up, Y^* always goes up faster than y^*.

When λ is higher, it takes an even longer time for y^* exceeding Y^* since the investment effect dominates, which reduces y^* as the project approaches the deadline. In addition, as σ further increases, Y^* strictly dominates y^*. On one hand, the project without time constraint can fully capture the option value. On the other hand, the

investment effect is strong with a higher λ. Thus $y^* \leq Y^*$ maintains for a longer period of time in this case.

Thus it can be concluded that the time-constrained project provides with more investment incentives when intensity λ is higher and when uncertainty σ is lower.

6.6 Policy implications

Several policy implications can be drawn from the model.

First, adding a time constraint in the advance purchase commitment contract will increase the incentive of earlier investments for two reasons. First, the investment flexibility of the pharmaceutical companies are restricted since the time constraint itself is as long the companies could wait. However, for the project without time constraint, the decision maker could wait until the option value is fully realized before investment. One can even choose to wait forever if the condition is not favorable enough. Second, a time constraint increases the risk of failure when the project is close to the deadline and forces the investors to start the project earlier, especially when the probability of success is low which is represented by "λ" in the model.

Second, if the authority has already determined to add a time constraint in the advance purchase commitment contract, dependent on the success probability of the project, the length of the time constraint should be chosen such that the investment effect is larger than the gamble effect for most of the time during the contract length. For the project with lower success probability, the contract length is better set to be moderately higher so that the companies have enough time to make sure the project will be successful after investment. Or the company will have to wait until the revenues are high enough (the gamble effect) so that it is possible for them to start the project. For the project with higher success probability, a short contract length will help increase the incentive of earlier investment. The reason is that the decision makers of these projects can well adapt to the pressure of a short time constraint by starting the project earlier instead of resorting to the gamble effect. Thus when it

is close to the deadline, they will not further delay investment but to invest sooner. Moreover, the longer the contract length, the less effect that time constraint will have exerted on the decision makers.

6.7 Conclusions

In this chapter we develop a model to value a pharmaceutical R&D project based on the real options approach. The sudden success of the project is modeled by a Poisson process where time-to-expiration is also taken into account. It is found that when the project is of limited time horizon, the intensity of the Poisson process does not simply add to the discount rate as in many other models, that either has infinite time horizon or consider catastrophic events. The intensity can be the decisive factor in determining the optimal investment threshold in that the success probability of the project is affected. Thus the impression that the intensity only increases the discount factor can be misleading in particular problems.

We also analyze how the optimal investment threshold of the time-constrained project changes with respect to the life remaining of the project $T-t$, the intensity of the Poisson process λ and the uncertainty of revenues σ. The model shows that the optimal investment threshold is determined by the balance of two effects: the investment effect and the gamble effect. The investment effect will reduce the optimal investment threshold while the gamble effect will increase it. Both effects get stronger as $T-t$ decreases. When it is close to the deadline, on one hand, the investment effect is stronger since earlier investment will leave more time for the R&D process, thus the project has higher success probability. On the other hand, the gamble effect is also stronger since the success probability is extremely low at this point. The only possibility that the investment will ever take place is the revenues are high enough if the project happens to be successful, which leads to waiting and late investment.

The intensity λ represents the average number of jumps that happen within a unit time, and a lower λ implies that the happening of the jump is lower. When λ is

extremely low, earlier investment is not a good strategy since the probability of the jump happening within the deadline is still low, while the opportunity of investing at high revenues is given up soon. Thus the investment effect is weaker when λ is of low values. The uncertainty of revenues σ is positive related to the gamble effect. A higher σ will increase the probability of Y_t reaching a higher value, which increases the incentives of the decision maker to wait when the project is close to the deadline.

The numerical results show that the time-constrained project does provide with more investment incentives when intensity λ is higher and when uncertainty σ is lower, i.e., when the investment effect is stronger and the gamble effect is weaker. Thus, adding a term in the advance purchase commitments, which states that the drug development process must be finished within a limited time, could be a good way to further increase the investment incentives of the private companies to tackle the problem of Neglected Tropical Diseases (NTDs) in the developing countries.

6.8 Appendix

Proof of Proposition 6.1

Consider the decision maker is at time t, the NPV of the project is

$$\begin{aligned} F(Y_t) =& E_{Y_t}\left[\int_0^{\bar{\tau}} e^{-\rho t}(-C)dt + \int_{\bar{\tau}}^{\infty} e^{-\rho t} Y_t dt - I\right] \\ =& \frac{C\left(e^{-\rho\bar{\tau}}-1\right)}{\rho} + \frac{Y_t}{\rho-\mu}e^{-(\rho-\mu)\bar{\tau}} - I. \end{aligned} \tag{6.37}$$

Since $\bar{\tau}$ is a random variable at time t which is exponentially distributed, the above function can also be treated as a function of $\bar{\tau}$, i.e., $F(\bar{\tau})$. The NPV of the project can be computed by taking the expectation of $F(\bar{\tau})$,

$$\begin{aligned} E\left(F(\bar{\tau})\right) =& \left[\left(\frac{C}{\rho}\int_0^{\infty} e^{-\rho x}\lambda e^{-\lambda x}dx\right) - \frac{C}{\rho}\right] + \left[\frac{Y_t}{\rho-\mu}\int_0^{\infty} e^{-(\rho-\mu)x}\lambda e^{-\lambda x}dx\right] - I \\ =& \left[\frac{C}{\rho}\left(\frac{\lambda}{\rho+\lambda}\right) - \frac{C}{\rho}\right] + \left[\frac{\lambda Y_t}{(\rho-\mu)(\rho+\lambda-\mu)}\right] - I \\ =& \frac{\lambda Y_t}{(\rho-\mu)(\rho+\lambda-\mu)} - \left(\frac{C}{\rho+\lambda} + I\right) \\ :=& G(Y_t). \end{aligned} \tag{6.38}$$

The proof is complete. ■

Proof of Proposition 6.2

Consider the decision maker is at time t, the NPV of the project is

$$\begin{aligned} f(Y_t,t) =& E_{Y_t}\left[\int_0^{\bar{\tau}} e^{-\rho t}(-C)dt + \int_{\bar{\tau}}^{\infty} e^{-\rho t}Y_t dt - I\right] P(\bar{\tau} < T-t) \\ &+ E_{Y_t}\left[\int_0^{T-t} e^{-\rho t}(-C)dt - I\right] P(\bar{\tau} \geq T-t) \\ =& \left[\frac{C\left(e^{-\rho\bar{\tau}}-1\right)}{\rho} + \frac{Y_t}{\rho-\mu}e^{-(\rho-\mu)\bar{\tau}} - I\right]\left(1-e^{-\lambda(T-t)}\right) \\ &+ \left[\frac{C\left(e^{-\rho(T-t)}-1\right)}{\rho} - I\right] e^{-\lambda(T-t)}. \end{aligned} \tag{6.39}$$

Since $\bar{\tau}$ is a random variable at time t which is exponentially distributed, the above function can also be treated as a function of $\bar{\tau}$, i.e., $F(\bar{\tau},t)$. The NPV of the project can be computed by taking the expectation of $f(\bar{\tau},t)$,

$$\begin{aligned} E\left(f(\bar{\tau}),t\right) =& \left[\left(\frac{C}{\rho}\int_0^{\infty} e^{-\rho x}\lambda e^{-\lambda x}dx\right) - \frac{C}{\rho} + \frac{Y_t}{\rho-\mu}\int_0^{\infty} e^{-(\rho-\mu)x}\lambda e^{-\lambda x}dx - I\right] \\ &\times\left(1-e^{-\lambda(T-t)}\right) + \left[\frac{C\left(e^{-\rho(T-t)}-1\right)}{\rho} - I\right] e^{-\lambda(T-t)} \\ =& \left[\frac{\lambda Y_t}{(\rho-\mu)(\rho+\lambda-\mu)} - \left(\frac{C}{\rho+\lambda}+I\right)\right]\left(1-e^{-\lambda(T-t)}\right) \\ &+ \left[\frac{C\left(e^{-\rho(T-t)}-1\right)}{\rho} - I\right] e^{-\lambda(T-t)} \\ :=& g(Y_t,t). \end{aligned} \tag{6.40}$$

The proof is complete. ■

Proof of Proposition 6.3

Since it is assumed that

$$F^*(y,t) = W(\log(y),t) = W(x,t), \tag{6.41}$$

$x^*(t)$ maximizes $W(x,t)$ if

$$\frac{\partial W(x^*(t),t)}{\partial x^*(t)} = 0 \quad or \quad \frac{\partial W(\log(y^*(t)),t)}{\partial \log(y^*(t))} = 0 \tag{6.42}$$

and

$$\frac{\partial^2 W(x^*(t),t)}{\partial x^*(t)^2} < 0 \quad or \quad \frac{\partial^2 W(\log(y^*(t)),t)}{\partial \log(y^*(t))^2} < 0. \tag{6.43}$$

Hence,

$$\begin{aligned} \frac{\partial F^*(y^*(t),t)}{\partial y^*(t)} =& \frac{\partial W(\log(y^*(t)),t)}{\partial y^*(t)} \qquad (6.44)\\ =& \frac{\partial W(\log(y^*(t)),t)}{\partial \log(y^*(t))} \times \frac{\partial \log(y^*(t))}{\partial y^*(t)} \\ =& \frac{\partial W(\log(y^*(t)),t)}{\partial \log(y^*(t))} \times \frac{1}{y^*(t)} \\ =& 0. \qquad (6.45) \end{aligned}$$

Thus it is proved that the first partial derivative of $F^*(\cdot)$ with respect to y at the point $y = y^*(t)$ is zero.

In addition,

$$\begin{aligned}\frac{\partial^2 F^*(y^*(t),t)}{\partial y^*(t)^2} =& \frac{\partial^2 W(\log(y^*(t)),t)}{\partial y^*(t)^2} \qquad (6.46)\\ =& \partial\left(\frac{\partial W(\log(y^*(t)),t)}{\partial y^*(t)}\right)/\partial y^*(t)\\ =& \partial\left(\frac{\partial W(\log(y^*(t)),t)}{\partial \log(y^*(t))}\times\frac{1}{y^*(t)}\right)/\partial y^*(t)\\ =& \left(\frac{\partial^2 W(\log(y^*(t)),t)}{\partial \log(y^*(t))^2}\frac{1}{y^*(t)^2}\right)\\ =& <0. \qquad (6.47)\end{aligned}$$

Thus it is also proved that the second partial derivative of $F^*(\cdot)$ with respect to y at the point $y = y^*(t)$ is negative. Hence $F^*(\cdot)$ is maximized when $x = x^*(t)$. ■

Chapter 7

Conclusions

I conducted a series of studies on three problems in the pharmaceutical industry. Each problem is discussed by comparing two models in every chapter. For the two models, one is unconstrained and serves as the benchmark. The other is limited by some condition that mimics the problem in real life. By comparisons, we have three major findings. First, the commercialization flexibility will incentivize earlier investments when uncertainty is low and it delays investment when uncertainty is high. Moreover, faster approval policy is more effective when uncertainty is low. Second, the social planner's project is more desirable in terms of early investment thus earlier access to the product, as well as a larger overall value of the project. While the project run by a Private-Public Partnership is a better option in terms of the flexibility to adjust the product's quality, but with the cost of delaying commercialization. Last, the contract with a time constraint on the R&D process will increase the probability of investment and lead to earlier investment, when investment effect dominates the gamble effect.

However, the models are simplifications of the real situations, further researches can be done on implementing more factors in practice.

First, in real life, the R&D process is far from observing the fluctuation of the underlying stochastic process but more complicated. It is usually composed of three or four phases of clinical trials before the start of commercialization. At certain point

in time, future decisions are usually made based on all the information available up to that time. In other words, the information is not Markovian as we have assumed in the thesis. Moreover, it is highly likely that the project is considered to be not promising and thus it can be abandoned to avoid losses in the future. In our models, we either assume that the project will be successful for sure or the costs will be paid till the end of the project even if it fails. If the abandonment option is implemented, the value of the project will further go up and thus the project should provide with more investment incentives.

Second, we assume that there is only one project in each models and the decision makers are endowed with only two choices which are to invest or to give up the opportunity. Hence the investment decision is made with no other opportunity costs besides discounting. However, in reality, the decision maker may have a portfolio of projects at hand with limited budget. In this case, the decisions made for the one project will definitely be affected by other projects in that portfolio since the goal of the decision maker is no longer maximizing the value of a single project but the portfolio.

Third, we assume that the project is only made for the particular decision maker with no other competitors. In a competitive industry, the first-mover advantage or late-mover advantage will need to be considered. The optimal investment timing does not only depend on the balance of the option value and NPV of the project, but also subject to the moves of other decision makers.

Fourth, further research can be done on analyzing the optimal length of the advance purchase commitments contract in chapter 6, in terms of the different goals that the government or the sponsor want to achieve. For instance, one goal can be to speed up investments thus the patients can have earlier access to the product, while only a medium quality of the product is required. Another goal is to invent a product of high quality while the timing of commercialization is not the priority. Or the government would want to balance the timing of commercialization with the product's quality. Dependent on the various goals, the contracts are optimal in different sense. Thus the optimal length of the contract will also be different.

Last, to capture more real life situations, the different ways that we model the pharmaceutical R&D projects could be combined, where any of the following factors such as investment lag, different growth rates before and after investment, commercialization flexibility, sudden success of the project and time constraint can be considered simultaneously. The analysis combining more factors can be done easier since some of the combinations have been throughly discussed in the thesis already.

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