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The Opportunity Cost of Capital: Development of New Pharmaceuticals

Ayman Chit, PhD[1,2], Ahmad Chit, CA[3], Manny Papadimitropoulos, PhD[2,4], Murray Krahn, MD[2], Jayson Parker, PhD[2], and Paul Grootendorst, PhD[2]

Abstract

The opportunity cost of the capital invested in pharmaceutical research and development (R&D) to bring a new drug to market makes up as much as half the total cost. However, the literature on the cost of pharmaceutical R&D is mixed on how, exactly, one should calculate this "hidden" cost. Some authors attempt to adopt models from the field of finance, whereas other prominent authors dismiss this practice as biased, arguing that it artificially inflates the R&D cost to justify higher prices for pharmaceuticals. In this article, we examine the arguments made by both sides of the debate and then explain the cost of capital concept and describe in detail how this value is calculated. Given the significant contribution of the cost of capital to the overall cost of new drug R&D, a clear understanding of the concept is critical for policy makers, investors, and those involved directly in the R&D.

Keywords

pharmaceutical, development, cost of capital, opportunity cost

Introduction

Innovation—the discovery of new ways to extract more value out of limited resources—is a primary determinant of our standard of living. Biopharmaceutical innovation is of particular importance given the contribution of new drugs to gains in longevity and health-related quality of life.[1] Most pharmaceutical research and development (R&D) is carried out by for-profit companies. The primary function of these companies is to translate biomedical knowledge, much of which is generated in academic and public sector labs, into new pharmaceutical drugs and vaccines. This involves drug discovery, drug development, clinical testing, manufacturing, and marketing. Pharmaceutical R&D—like other forms of R&D—is not free; it is resource intensive. Moreover, drug R&D is both risky and time-consuming. Many drug development projects fail and there is a lag between expenditure outlays and the receipt of sales revenues for the drugs that succeed.

There is a surprising amount of debate regarding the resource cost of bringing a new drug to market. Widely cited articles by DiMasi and colleagues measures the real (inflation-adjusted) cost in the billions of dollars, and, unfortunately, they find this cost is rising exponentially.[2-5] Others place the cost orders of magnitude lower.[6-10] There are also suggestions that widely cited estimates of the cost of new drug development are artificially inflated for political reasons.[11]

Financing costs are a key component of the DiMasi cost estimates and account for about half of total costs. These financing costs, essentially interest on the money ("capital") tied up during the lengthy and risky R&D process, are particularly contentious. DiMasi and colleagues use interest rates ("cost of capital") as high as 11.5%.[2,3] Some commentators suggest that they are zero,[11,12] whereas others are ambivalent, but suggest that if there is a cost of capital, then it is as low as 3%.[6] The choice of interest rate has a dramatic effect on the total cost of developing a new drug, given the lag between the outlays on R&D and the point at which sales revenues accrue. For instance, at 11%, a US$1 outlay accrues about US$4 interest after 15 years, but only US$1 interest at 5% (Figure 1).

Given this controversy, our goal here is to adjudicate on the debate, identify the arguments used by proponents on either side of the debate and evaluate their claims, and finally assess how the cost of capital is estimated.

[1]Sanofi Pasteur, Toronto, Ontario, Canada
[2]University of Toronto, Ontario, Canada
[3]Deloitte Touche Tohmatsu Limited, Canada.
[4]Eli Lilly and Company, Canada.

Corresponding Author:
Ayman Chit, Sanofi Pasteur, 1755 Steeles Ave West Toronto, ON Ontario M2R 3T4 Canada.
Email: ayman.chit@sanofipasteur.com

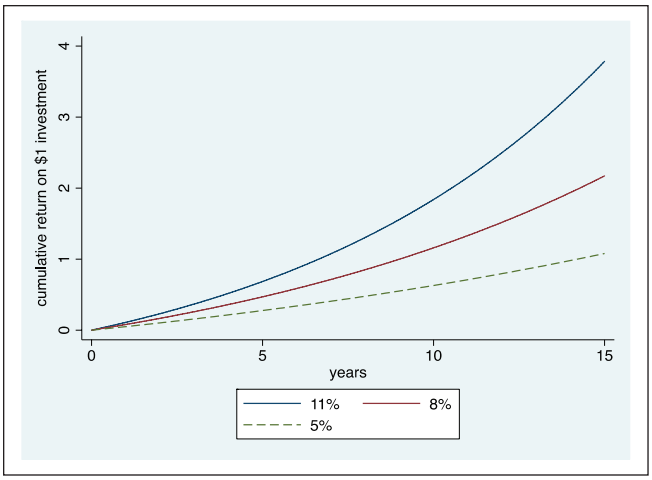

Figure 1. Cumulative return on US$1 investment, compounded annually, by years since investment and by percentage rate of return.

What Is the Cost of Capital?

The cost of financing pharmaceutical R&D is the return needed to entice funders to commit resources to pharmaceutical R&D instead of other investments. The underlying idea is that investors will only commit resources if they expect to receive an amount that they can earn on other equally risky investments. The amount that can be obtained elsewhere constitutes the investor's "opportunity cost" of capital.

The notion of the opportunity cost of capital is widely accepted within economics, although, as we discuss below, the methods used to estimate its value are contested. But some outside of economics, and even some economists themselves, dispute the concept. In particular, the noted academic physicians Relman and Angell[12] and Angell[11] suggest that there is no opportunity cost of capital because pharmaceutical firms "have no choice but to spend money on R&D if they wish to be in the pharmaceutical business."[11(p45)] This statement is correct, as far as it goes. But investors will provide funds to any venture only if they anticipate receiving sufficient compensation for delaying consumption and incurring the risk of potentially losing some or all of their capital. Investors in pharmaceutical firms, that is, shareholders, only wish to be in the pharmaceutical R&D business if they receive as much in compensation as they do in other equally risky ventures. Microeconomist David Friedman explains the underlying theory (p. 205):

> A steel mill cannot be converted into a drainage canal—but an investor can decide whether he will use his savings to pay workers to build the one or the other. So the anticipated return on all investments—the interest rate—must be the same. If investors expected to make more by investing a dollar in building a steel mill than by investing a dollar in digging a drainage canal, capital would shift into steel; the increased supply of steel would drive down the price of steel and the return on investments in steel mills. The reduced supply of capital in canal building would, similarly, increase the return on investments in canals. Investors would continue to shift their capital out of the one use and into the other until the returns on the two were the same (p. 205).[13]

It is instructive to assess the consequences to firms that fail to generate sufficient returns. Drug companies can raise funds to finance R&D projects from several sources. First, they can use retained earnings, that is, gross profits generated on sales of their existing drugs that are not returned to shareholders in the form of dividends. Second, they can borrow funds from lenders in the bond market. Third, the company can sell stock that it itself holds, or issue new shares of the company (diluting the value of existing shares). If firms are unable to develop new drugs that drug plans and consumers are willing to pay for, either from bad luck[14-18] or incompetence, then their pool of retained earnings will eventually dry up. Lenders will be hesitant to lend money, or will demand a substantial risk premium, if they perceive the default risk to be high. The company's share price, a harbinger of future profits, will decline, reducing the revenue potential from selling new or existing stocks. Such a company will eventually go bankrupt or be at risk of takeover by another firm that believes the company is being mismanaged. The firm pursuing the takeover buys as much stock as possible, enough to let it take over the company, fire most of its executives, and install competent replacements. If the firm is successful, earnings and the market value of the company's stock both shoot up.[13]

Light and Warburton[6] also take issue with the notion that the opportunity cost of capital is a legitimate resource cost. They write,

> . . . experts argue that innovative companies must do R&D, and this is a regular cost of doing business; so estimated profits foregone should not be added to out-of-pocket costs . . . If revenues are coming in from other products, then the [R&D] costs are recovered as one goes along. (p. 8)

This argument again fails to recognize that retained earnings, like other types of investment funds, have a variety of valuable uses. If those with a claim to the retained earnings (ie, shareholders) do not anticipate generating sufficient gross profits from pharmaceutical R&D, they will move their funds to other ventures. The secular decline in antibiotic drug development is a telling illustration; this decline reflects, in part, reduced anticipated sales revenues owing to antibiotic stewardship initiatives on the part of prescribers and a commensurate shift to other therapeutic classes.[19,20]

Light and Warburton[6] further state, "Even if one were to accept the argument that profits foregone should be included as a 'cost,' US government guidelines call for using 3 per cent, not the 11 per cent used by DiMasi and colleagues."

(p. 164) Three percent might be the appropriate cost of capital for government, but the return required for private investors contemplating allocating funds to pharmaceutical ventures is, as we discuss in further detail below, much higher. Indeed, most studies place the private cost of capital for the pharmaceutical industry to be 8% or higher.[21]

Estimating the Private Cost of Capital

How is a drug company's cost of capital estimated? One must first determine how much of the company's operations are financed by debt (capital from bondholders) versus equity (capital from shareholders). The relative amounts of debt and equity financing within a public company can be ascertained by reviewing public financial reports, which by law must disclose the relative amounts.

The opportunity cost of the two sources of funds is different. The opportunity cost of debt is simply equal to the preset interest rate agreed to between the corporation and its lenders (bondholders). Shareholders face more variable returns than lenders; there is no predetermined return on investments and, in the event of insolvency, shareholders are paid last. To estimate the opportunity cost of financing projects through shareholder equity, the investment community relies on financial models. Chief among these is the capital asset pricing model (CAPM). The CAPM was developed by William Sharp in 1964, and remains the dominant model today.[22] The key articles by DiMasi and colleagues all estimated the cost of capital using this approach.

CAPM estimates the opportunity cost of investing in firm *i*, also known as firm *i*'s "cost of equity capital," as the sum of the risk free rate of return (RFR), normally measured as the return on US government bonds, and firm *i*'s equity risk premium. Formally, according to the CAPM, $E(R_i)$, the expected cost of equity capital for firm *i* is

$$E\left(R_{\mathrm{i}}\right) = \mathrm{RFR} + \beta_{\mathrm{i}}\left(E\left(\mathrm{RM}\right) - \mathrm{RFR}\right).$$

β_i, the "beta" for firm *i*, determines firm *i*'s equity risk premium; firms with larger beta values require larger returns. Firm *i*'s beta reflects the historical correlation between the returns on firm *i*'s shares and the returns from the stock market as a whole. The expected market-wide return, $E(\mathrm{RM})$, is subject to undiversifiable risks, such as the risks that come from macroeconomic downturns. If firm *i*'s returns are highly correlated with returns in the stock market as a whole, then firm *i*'s beta will be large. This would be the case, for instance, if firm *i* produces a good or service whose sales are particularly sensitive to macroeconomic shocks. A good example is a firm that rents out construction equipment; such a firm faces undiversifiable risks that are greater than that of the stock market as a whole. Conversely, a firm with a beta of zero means that the firm's share returns are completely uncorrelated with the market returns. Sales of such a firm are insulated from the market-wide systemic risk. Thus, in summary, a firm's cost of equity capital depends on the risk free rate—the higher this is, the higher the opportunity cost to the investor of assuming the risks of holding equities—and firm *i*'s equity risk premium, which measures the sensitivity of firm *i*'s returns to the market-wide systemic risks.

The forgoing describes the cost of equity capital for a particular firm. The cost of equity capital for an industry can be estimated with the same formula, by weighting the individual firms' betas by the relative market value of each firm in the industry. Beta statistics can also be calculated by sector. Damodaran[23] recently estimated the beta for the US health care products sector as a whole as 0.99. Thus, health care product suppliers have a risk profile that is close to the stock market average. Pharmaceutical firms have betas that are slightly higher, 1.03. Biopharmaceutical firm betas are 1.10. Construction supply firms have betas of 1.60. Beta values for public companies are routinely reviewed and updated for use by investment portfolio managers and others in the financial sector. These values are periodically published by various financial reporting companies such as *Thomson Reuters*,[24] *Morningstar*,[25] and *Bloomberg*.[26]

The cost of capital that firm *i* faces is the weighted average of the cost of debt capital and the cost of equity capital. The pharmaceutical industry relies almost exclusively on equity capital,[2-4,10] so the cost of capital for the industry mirrors the cost of equity capital. This is because, pharmaceutical firms specifically, and technology companies more generally, contend with market imperfections that makes borrowing unattractive to them.[27] The problem is one of information asymmetry between the pharmaceutical firm and its potential lenders. Given the technical nature of pharmaceutical technology, the firm will always have a better grasp of the quality and riskiness of their projects than potential lenders. This causes lenders to ask for a premium above what they would charge firms with a more lucid set of business projects. The fact that very few pharmaceutical firms take any debt at all indicates that the cost of debt is too high; otherwise, many firms would take advantage and leverage the expansion of operations and R&D through affordable debt.

Of course, not all of the resources that the industry consumes are financed privately. Governments also finance a portion of industry-sponsored pharmaceutical R&D via tax subsidies. And the cost of capital for government—estimated to be in the range of 3% to 7% for developed countries[28]—is lower than that for private companies. This government cost of capital is essentially equal to the RFR described earlier. Corporations and government contributed 57% and 39%, respectively, of the total biomedical R&D spend in the United States over the period 1999-2008, with the remaining 4% coming from charitable donations.[29] Most of the government support is focused on early-stage discovery R&D; DiMasi[3] suggests that tax credits contribute only a small amount of the in industry directed R&D.

What, then, are we to make of the cost of industry capital estimates that account for about half of DiMasi and colleague's estimated cost of bringing a new drug to market? Our reading of the literature is that, if anything, these estimates are conservative. The reason is that the CAPM model, which was used to generate estimates of the pharmaceutical industry cost of equity capital, tends to provide conservative estimates. In particular, other models, which relax some of the assumptions underlying the CAPM model, tend to produce higher cost of capital estimates. For instance, the leading competitor to the CAPM model, the Fama and French (F-F) 3-factor model, considers company size and company "health" beyond just what is included in CAPM. The F-F model produces higher risk premia for smaller companies and for companies that are judged to be in poor "health," as measured by a relatively high book equity to market equity ratio. Indeed, Vernon and colleagues have compared cost of capital estimates using CAPM and F-F and found the latter would produce higher costs of capital.[30]

As another example, Giaccotto et al relax another of the CAPM assumptions, and again obtain higher estimates of the cost of equity capital. The assumption they relax concerns the unique time profile of sales revenues of pharmaceutical firms, with sales growing over time until generic firms enter, at which time sales drop markedly. The CAPM implicitly assumes that sales follow a random walk. The authors find that relaxing this assumption increases the cost of capital for some pharmaceutical firms by as much as 2.8%.[31]

In conclusion, capital is a scarce resource and, like any other scarce resource, there is an opportunity cost associated with its use. The opportunity cost of capital invested in drug discovery, development and commercialization is the return required to compensate investors to invest in time-consuming and risky R&D. There are standard methods in the field of finance to produce estimates of the opportunity cost of capital for various firms and sectors of the economy. The pharmaceutical cost of capital estimates used by DiMasi and colleagues are consistent with both economic theory and financial accounting practice.

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