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DRUG DEVELOPMENT COSTS WHEN FINANCIAL RISK IS MEASURED USING THE FAMA–FRENCH THREE-FACTOR MODEL

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SUMMARY

In a widely cited article, DiMasi, Hansen, and Grabowski (2003) estimate the average pre-tax cost of bringing a new molecular entity to market. Their base case estimate, excluding post-marketing studies, was $802 million (in $US 2000). Strikingly, almost half of this cost (or $399 million) is the cost of capital (COC) used to fund clinical development expenses to the point of FDA marketing approval. The authors used an 11% real COC computed using the capital asset pricing model (CAPM). But the CAPM is a single factor risk model, and multi-factor risk models are the current state of the art in finance. Using the Fama–French three factor model we find that the cost of drug development to be higher than the earlier estimate. Copyright © 2009 John Wiley & Sons, Ltd.

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In a widely cited article, DiMasi *et al.* (2003) estimate the average pre-tax cost of bringing a new molecular entity (NME) to market. Their base case estimate, excluding post-marketing studies, was $802 million (in $US 2000). Strikingly, almost half of this cost (or $399 million) is the cost of capital (COC) used to fund clinical development expenses to the point of FDA marketing approval. The authors used an 11% real COC computed using the capital asset pricing model (CAPM). But the CAPM is a single-factor risk model, and multi-factor risk models are the current state of the art in finance. In particular, the three-factor model developed by Fama and French (1993) is now widely used to estimate COC. In addition to the market risk factor used in the CAPM, the Fama–French model includes size and book-to-market risk factors, and these additional risk factors can produce very different COC estimates compared to CAPM estimates. For this reason, and because the capital cost component of the DiMasi *et al.* estimate is large, we decided to update the cost of drug development using a real COC obtained using the Fama–French model. For comparison, we also estimate the COC using the CAPM for our data sample.

To estimate our models, we collected firm financial data from Standard and Poor's Compustat data and securities returns data from the Center for Research on Securities Prices (CRSP). We obtained the Fama–French annual factors covering 1927–1980 from Kenneth French's (2007) website. We computed the average for the factors during this period as estimates of the expected factor risk premiums. Using

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this long period provides more precise estimates and is particularly appropriate in our case because we are estimating the COC for drug projects that take an average of 12–15 years to develop, and produce cash flows for another 20 years. We estimated the factor loadings (risk sensitivities) for all pharmaceutical firms (SIC 2834 according to Compustat) with at least three years of CRSP return data ending in 1980. We use no more than 10 years of data ending in 1980 to allow enough data for precise estimates but not so much that the firm's risk could have substantially changed during the estimation period. We then applied each firm's factor loadings to the factor risk premiums to compute their COCs, and then averaged firms' COCs to obtain an industry COC.

We used data up to 1980 because that was the beginning of the period in which drugs in the DiMasi *et al*. sample were beginning to be researched and developed. Their sample period covers 1980 to 1999. According to Grabowski *et al*. (2002), drugs that gained marketing approval between 1990 and 1994 were discovered and underwent preclinical and clinical research starting in 1980 on average (DiMasi *et al*., 2003). COC estimates including data up through the 1990's had virtually no impact on our results. Indeed, in their original paper, DiMasi *et al*., report that the CAPM COC estimates remained largely constant through the 1980's and 1990's. We also found this to be true.

Our results are reported below along with a brief discussion of our findings. Note that these are actually estimates of equity COC. But because the average firm in the industry had very little debt during our sample period, equity COC is effectively firm COC. The effect of adding debt would be to lower slightly both the CAPM and Fama–French COCs. Because the main point we make here is based on the difference between these COC estimates, debt would have no effect on our results. We find that the average real COC for the pharmaceutical industry is 11.02% using the CAPM and 14.36% using the Fama–French model.[1] The 3.34% COC difference has two significant effects on the net present value of pharmaceutical R&D investments. First, the annual costs of R&D compound at a higher rate over the 12–15 years of pre-clinical and clinical development. Second, the present value (at the time of market launch) of the net cash flows produced for 20 years is substantially reduced.

Why do our COC estimates from the Fama–French model exceed the CAPM estimates for pharmaceutical firms? We find that the pharmaceutical industry is exposed to more size-related risk than the average industry. For example, the average industry has a 0.39 size-factor loading, compared to 0.67 for the pharmaceutical industry. Note that size risk is not purely based on company size but rather on the types of risks often faced by small firms. Pharmaceutical R&D projects have very skewed payoffs, and this could account for their extra size risk, even though the firms themselves are not particularly small. Like many small firms, even relatively large pharmaceutical firms often rely on external equity funding. If their pipeline is unproductive for even a few years, they jeopardize their ability to obtain the financing that they need to survive.

Table I compares results using the CAPM and Fama–French models. Average capitalized R&D costs are computed by compounding expected out-of-pocket R&D expenditures at either the CAPM or Fama–French COC.

For comparison, we include the data up through 2006 to see if the difference in COCs persists. Indeed, we find that the difference widens. The average CAPM COC for the industry falls to 10.39%, while the Fama–French COC rises to 16.61. We find that the spread widens largely because the average size-factor loading increases from 0.66 to 0.99.

Figure 1 shows the net after-tax revenues discounted at the Fama–French COC. Raw R&D figures and net revenues data are from Grabowski *et al*. (2002), with the later covering drugs that obtained marketing approval between 1990 and 1994. The level of after-tax present value net revenues is shown for each profitability decile of NMEs, from the most profitable, to the least. Figure 1 is a reconstruction

[1]Other researchers have also found that firm hurdle rates are typically higher than those generated by the CAPM (Poterba and Summers, 1995). A 2001 informal survey of six pharmaceutical firms reported a range of nominal COC values between 13.5 and 20%, which based on a 3% expected inflation rate yields a real COC range from 10.5 to 17% (Grabowski *et al*., 2002).

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Table I. Cost of capital and average capitalized R&D costs

Model	Real cost of capital (%)	Pre-tax cost per NME
CAPM	11.02	$803.3 Million ($US 2000 values)
Fama–French	14.36	$992.2 Million ($US 2000 values)

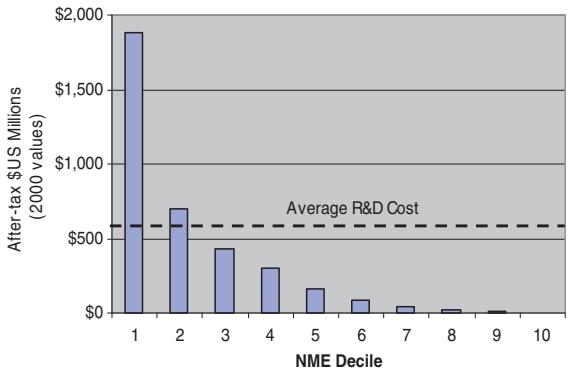

Figure 1. Distribution of after-tax present value net revenues by NME decile and average after-tax R&D costs

of Grabowski *et al*. (2002) Figure 7 using our Fama–French COC. On an after-tax basis, using an effective corporate tax rate of 33% (Grabowski *et al*., 2002), the Fama–French-based estimate of average R&D costs per NME is approximately $664 million; higher than 8 of the 10 NME decile's after-tax present value net revenues.

In conclusion, our results show that only about 20% of NMEs cover their average capitalized R&D expenses when R&D expenses are capitalized at the industry average Fama–French COC rate. When Grabowski *et al*. (2002) use the industry average CAPM COC rate of 11%, they find that about 30% of NMEs cover their average capitalized R&D expenses. But the exact percent of NMEs covering R&D costs is not our focus. Rather, our main point is to show that when pharmaceutical risk is measured using the Fama–French multi-factor risk model, industry COC exceeds that obtained using the single-factor CAPM.

Are there cases where firms would have made different R&D investment decisions if they had used Fama–French COCs instead of their currently adopted COCs? We were unable to obtain the COCs used for individual R&D projects from firms because the firms we contacted consider their COCs to be proprietary information. But according to Graham and Harvey's (2001) widely cited survey, 73.5% of chief financial officers always or almost always used the CAPM to compute the COC that they used to select projects. Had those chief financial officers used a larger Fama–French COC instead of a CAPM COC, at least some marginal projects would be rejected that would otherwise have been accepted.

But we have no way of measuring the number and magnitude of the pharmaceutical R&D projects that might be affected. We suspect that pharmaceuticals that face tighter price constraints, either by market competition or by government or health plan policy, would be most affected. These medicines are less likely to provide the larger returns required by the Fama–French approach.

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REFERENCES

DiMasi JA, Hansen R, Grabowski HG. 2003. The price of innovation: new estimates of drug development costs. *Journal of Health Economics* **22**: 141–185.

Fama EF, French KR. 1993. Common risk factors in the returns on stocks and bonds. *Journal of Financial Economics* **33**: 3–56.

French KR. 2007. *Data Library*, http://mba.tuck.dartmouth.edu/pages/faculty/ken.french/data_library.html.

Grabowski HG, Vernon JM, DiMasi JA. 2002. Returns on research and development for 1990s new drug introductions. *PharmacoEconomics* **20**(Suppl. 3): 11–29.

Graham J, Harvey C. 2001. The theory and practice of corporate finance: evidence from the field. *Journal of Financial Economics* **60**: 187–243.

Poterba JM, Summers LH. 1995. A CEO survey of U.S. companies time horizons and hurdle rates. *Sloan Management Review* (**Fall**) **37**(1): 43–53.

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