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The US$ 1 billion drug. A fairytale.

It takes US$ 802 Mio to take one drug successfully to market. This was Joseph DiMasi's central message in his article in 2003 about R&D costs. This number has been cited many times and has been abused in many ways. US$ 802 Mio should discourage any rational investor from investing into drug development. In 2007 DiMasi rerun his study with new data, especially with a new set of success rates. Overall success rates increased over the last years and moved from 21% to 30% from IND to approval, i.e. a drug entering clinical development has a 30% chance to reach market. But to our big surprise the new number on drug development costs even increased to an astonishing US$ 1,241 Mio per drug. We expected that an increase in the success rate translates into lower costs to bring at least one drug to market. To better understand what is behind DiMasi's figures we will deconstruct his misleading number in detail.

DiMasi's number does not refer to how much a company has possibly to spend to take its drug to the market. Neither does he say how much has been spent on the research and development for drugs that are on the market. No, DiMasi's numbers are the average expenses it takes to get one drug onto the market, taking into account all possible failures too. So, with a 21% success rate it takes already about 5 clinical phase I projects in order to reach the market with one compound. And in order to inflate the number a little more, DiMasi doesn't use a forward-looking perspective discounting future expenses, but capitalises all past expenses at the cost of capital of the companies.

For each clinical phase we have a mean estimate of costs, success rates, and duration. Furthermore, DiMasi claims that 65% (in 2007, in 2003 it was 69%) of all R&D expenses are spent for clinical trials. This means that per investigational new drug (IND) one has to account for US$ 60 Mio (in 2003 only US$ 26 Mio) for preclinical expenses. This means that a company has to invest on average US$ 60 Mio for R&D to generate one IND, e.g. to bring one drug into clinical development.

Table 1: DiMasi's parameters for clinical phases.

2003	Phase I	Phase II	Phase III	NDA	**TOTAL**
costs (US$ Mio)	15.2	23.5	86.3	0.0	**125.0**
success rates	71%	44%	69%	100%	**21%**
duration (months)	12.3	26.0	33.8	18.2	**90.3**
2007					
costs (US$ Mio)	32.3	37.7	96.1	0.0	**166.1**
success rates	84%	56%	64%	100%	**30%**
duration (months)	19.5	29.3	32.9	16.0	**97.7**

Table 1 displays the numbers for clinical development DiMasi has used. While the early development costs were high for his 2003 calculation, they become exorbitant for his 2007 calculation. This way the preferential increase of success rates cannot offset the enormous raise of cost assumptions. According to DiMasi the cost estimates are taken from a sample of the ten largest pharmaceutical companies. Of course, this is in no way representative. Biotech companies manage to run clinical trials at much lower expenses, throughout all phases.

The second point that inflates DiMasi's number is the fact that costs are not simply added up, but weighted

by the success rates. Table 2 indicates how many projects it takes in each phase to reach market with one project on average.

Table 2: Attrition weights.

2003	Phase I	Phase II	Phase III
Probability to reach market	21%	30%	69%
# it takes that one reaches market	4.7	3.3	1.5
2007			
Probability to reach market	30%	36%	64%
# it takes that one reaches market	3.3	2.8	1.6

The last important driver of DiMasi's number is the fact that he capitalizes all costs at the cost of capital (11% in 2003, 11.5% in 2007). Preclinical costs that lie far in the past therefore compounded over 10 years at 11%, which means that we do not only account for them 4.6 times because of the attrition weights, but we increase the value by another factor 2.8 because of the capitalisation of costs. An originally relatively reasonable number of US$ 26 Mio then contributes US$ 335 Mio to DiMasi's number. The final calculation by DiMasi is shown in figure 1.

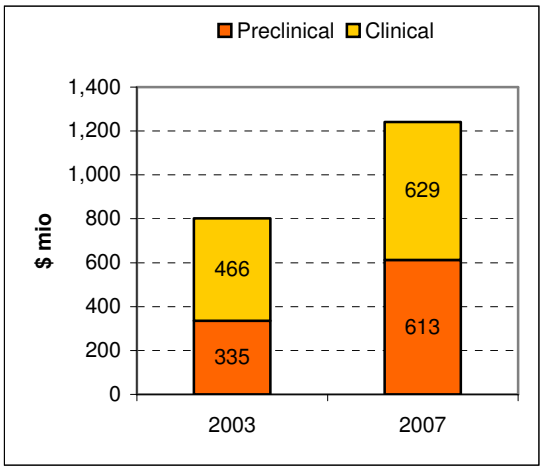

Figure 1: DiMasi's figures

While the 2003 number requires an average drug reaching US$ 310 Mio peak sales to break even (which is already far better than the vast majority of all drugs), the 2007 number requires peak sales of US$ 508 Mio. It means that one should abandon any project that is estimated to reach sales at its peak of less than US$ 508 Mio (using a standard sales curve). We can of course immediately see that most biotechs develop drugs with much smaller peak sales. DiMasi's figures are as already said in no way usable for other than big pharma companies.

DiMasi's numbers are correct in the way they are defined, but they have two serious flaws. First they are based on a sample of companies that follow the expensive blockbuster model, i.e. only big pharma is included. Therefore the cost estimates are far from being representative. Second, one wants to know how much he must spend, not how much he has spent. We therefore should rather discount the costs back to today than capitalize it from the past to today. Also, when talking about value, we should adjust all costs by their probability. In reality, no biotech will ever get funded by investors with a sum comparable to DiMasi's number. Biotechs can and do bring drugs on the market for less than US$ 100 Mio. DiMasi's number is only interesting for multinational pharmaceutical companies hunting for blockbusters. With this strategy currently failing and companies moving to targeted medicines,and personalized medicine, niche indications, and orphan indications, the costs for a successful drug launch need to be much lower resulting from much higher success rates.

Table 3 displays some more realistic assumptions about drug development. While we stick to DiMasi's 2003 numbers for success rates and duration, we have adapted

the clinical costs according to our experience.

Table 3: More realistic assumptions

	Phase I	Phase II	Phase III	NDA	**TOTAL**
costs (US$ Mio)	5	12	68	3	**88**
success rates	71%	44%	69%	100%	**21%**
duration	12.3	26	33.8	18.2	**90.3**

Table 4: Indicative numbers out of the three data sets

	2003	**2007**	**Avance**
Capitalized and attrition weighted[1]	466	629	261
Attrition weighted (out of pocket)[2]	274	364	162
Summed up[3]	125	166	88
Risk Adjusted (out of pocket)[4]	59	109	36
Discounted and risk adjusted[5]	45	79	25
Required peak sales[6]	311	509	231

Table 4 finally shows the various values we get out of these three data sets. We focus in this analysis only on the clinical costs. As we can see, the eye-catching US$ 629 clinical spendings of the 2007 data set can also be interpreted as US$ 79 Mio. We however think that this number can even be lowered to US$ 25 Mio, the risk adjusted present value of all investment to come for one specific drug. The pharmaceutical companies might be interested in advertising DiMasi's high number, entrepreneurs and investors alike might be more interested in the realistic value of the costs for one project (the US$ 25 Mio). The required peak sales allow judging which data set makes most sense.

[1] DiMasi's approach
[2] DiMasi's approach but without capitalisation of costs
[3] All costs summed up as they are, without adjustment for risk nor time
[4] All costs adjusted by the probability that they occur (i.e. multiplied by previous success rates)
[5] All costs adjusted for their risk and discounted at the cost of capital (11%) back to IND
[6] Minimum peak sales to reach an IRR higher than the cost of capital (preclinical costs included)