

What is the optimal portfolio structure?

The optimally balanced pipeline

In every larger pharmaceutical company management asks about the optimal portfolio structure. How can they make sure that the products that go off patent can be replaced with new, patent protected drugs? Let us first assume for simplicity that all drugs follow the dynamics as exhibited in table 1, i.e. have the same phase durations and success rates.

Table 1: Project dynamics.

	Phase 1	Phase 2	Phase 3	Submission
Success Rate	60%	37%	63%	79%
Duration (months)	18	29	42	18

Out of the success rates we can already deduce the probability of a project in a certain phase to get to the market. A phase 3 project for instance needs to pass phase 3 and submission and has therefore a probability of $63\% \cdot 79\% = 50\%$ to reach the market.

Table 2: Probability to reach market.

	Phase 1	Phase 2	Phase 3	Submission
Probability to reach market	11%	18%	50%	79%

From these probabilities we conclude, how many projects in which phase are necessary to get one project to the market. Since a phase 1 project has a probability of 11% to reach the market, we need about 9 ($=1/11\%$) phase 1 projects to get one project to the market on average. These 9 projects become about 5-6 phase 2 projects, or 2 phase 3 projects according to the success rates.

Table 3: Average number of necessary projects.

	Phase 1	Phase 2	Phase 3	Submission
Probability to reach market	9.1	5.4	2.0	1.3

But does that mean that a perfectly balanced pipeline should be weighted according to the numbers in table 3? The

answer is no, because the projects remain for different times in the phases. If we expect one approval every year, we need not only have 1.3 times as many projects in submission, because these would just lead to the one approval in that year. The projects for next year's approval should also already show up in the pipeline. Therefore we have to multiply the weights of table 3 with the respective length of the phases in years. This leads us to the balanced pipeline structure of figure 1.

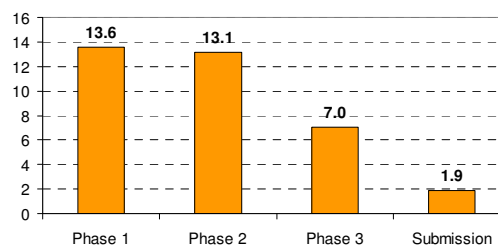


Figure 1: Optimal pipeline structure

If we assume that a project will have 12 years of patent protected sales, then we can deduct what pipeline should correspond to a certain portfolio of approved drugs. If there are 6 approved drugs still under patent protection, then we can expect about one approval every second year. The corresponding pipeline that is able to replace the current portfolio of drugs has half of the projects displayed in figure 1. In a different terminology we could say that the company requires a feed rate of about 7 ($\approx 13.6/2$) phase 1 projects, i.e. every year 7 projects should enter the clinical pipeline.

Of course a pipeline contains projects in various disease areas and the described weighting could be applied to its sub-pipelines in, let's say, cancer, inflammation, and endocrinology.

Effects of in-licensing

In a pharmaceutical company it is unrealistic to assume that all projects are self-originated. If the company in-licenses projects in phase 2, then these projects have never appeared in phase 1 in their pipelines. Accordingly the pipeline might look like in figure 2.

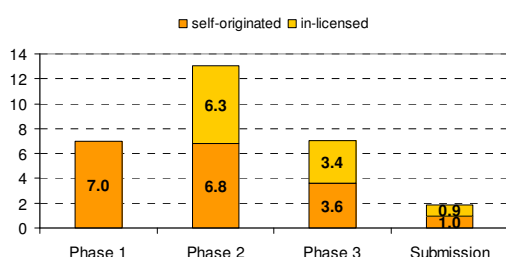


Figure 2: Optimal pipeline structure with in-licensing feed rate.

This mixed pipeline requires an average of 6.3 in-licensed projects in phase 2. This then corresponds to a feed rate of 2.6 projects every year (remember, phase 2 projects remain 29 months in phase 2).

Pipeline analysis

For analysts and managers alike the question of “How lucky has the company been so far” is quite intriguing. Imagine a company with the following pipeline¹:

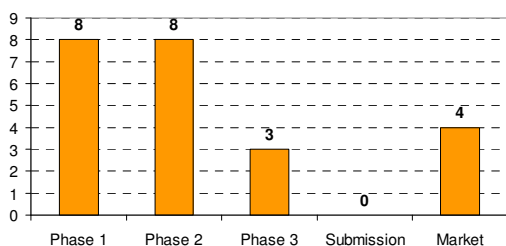


Figure 3: Current pipeline.

¹ We have chosen Genentech’s oncology pipeline. Second and higher indications have not been counted.

Is this a good or a bad pipeline, i.e. has the company been excessively lucky until now or is the perceived attrition about normal?

To answer this question, we have to model the pipeline with success rates and timelines in line for oncology projects.

Table 4: Oncology parameters.

	Phase 1	Phase 2	Phase 3 to Approval
Success Rate	75%	60%	80%
Duration (months)	20	29	33+16=49

Since most of Genentech’s projects are monoclonal antibodies we have chosen monoclonal antibody success rates (from Reichert²). Timelines are taken from DiMasi³.

The question is, what is the most likely feed rate for a company exhibiting a pipeline like in figure 3? It is clear that randomness is involved in the pipeline progression; first not every project moves to the next phase, and second, in the company’s scenario the success rates are not necessarily followed by the number. For the calculation we must assume a feed rate of preclinical projects, one phase earlier than our pipeline figures. Otherwise the feed rate must be 8 projects divided by 20 months (=4.8 projects/year). We are well aware that the feed of IND projects is also somewhat random, therefore we assume a constant feed rate one phase before the first

² Reichert, J. et al., „Monoclonal Antibody Successes in the Clinic“, Nature Biotechnology, September 2005.

³ DiMasi, J, et al., „The Cost of Biopharmaceutical R&D: Is Biotech Different?“, Managerial and Decision Economics, 2007.

phase we look at, allowing the preclinical success rate (65%) to act as “randomisation” to the IND feed rate. Furthermore we don’t look at the commercialised projects simply because the exhibited pipeline is a result of an increased R&D activity over the recent years and the number of commercialised projects does not reflect that.

Now we can attribute to the current scenario an exact likelihood following the steps as in table 5.

Table 5: Likelihood calculation.

	Phase 1	Phase 2	Phase 3
Probability (p)	65%	49%	29%
Duration (d)	1.67	2.42	4.08
Projects (n)	8	8	3
$P(\#projects=n)$	$p^n * (1-p)^{(feed*d-n)}$		
Combinations (C)	$(feed*d)! / ((feed*d-n)! * n!)^4$		
Total	$P1 * C1 * P2 * C2 * P3 * C3$		

With this combinatorial calculation we can then assess the likelihood of different feed rates as displayed in figure 4.

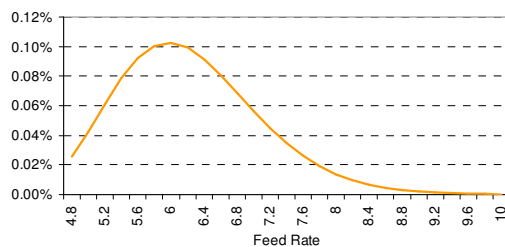


Figure 4: Likelihood of current scenario given different preclinical feed rates.

Apparently a preclinical feed rate of 6 maximises the likelihood of the current pipeline, i.e. the current pipeline is a more realistic scenario if we assume a feed rate of 6 preclinical projects than only 5 or 6.5. What does that mean?

If the actual preclinical feed rate of the company is less than 6, then the company currently manages to keep attrition lower than the industry average. One can interpret this as operational excellence, in which case could increase the success rates until the most likely feed rate matches the observed one. This is a method of success rate calibration specific to the company. On the other hand, if we do not believe that some companies can reach higher success rates than others in the long run, this means that the company has just been excessively lucky in the recent years.

⁴ Since the factorial function is only available for integer numbers and the feed rate, representing an average number, can also be non-integer, we need to use the Gamma function, an extension of the factorial function to non-integer numbers.