PROJECT CASE STUDY

QUANTITATIVE DISEASE AREA STRATEGY

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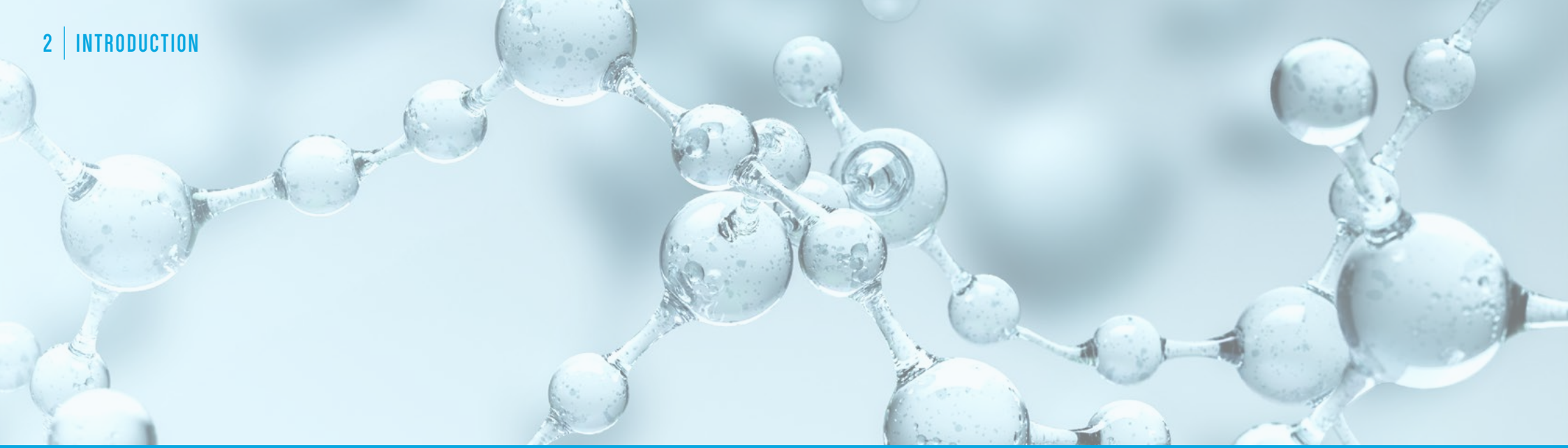
CAPTARIO



BACKGROUND

In this article I will present a case study on how we can use quantitative methods to influence or support disease area strategies.

The case study is based on recent client work, but the projects have been de-identified and I have also changed the data to avoid resemblance with actual projects.

I will start by describing the assets already in the portfolio, however, I am using spice names instead of real project names. First I will describe the baseline portfolio, and then show a couple of examples on how to assess improvement strategies.

BASE CASE

The portfolio currently consists of four assets under development:

1. Caper which could be considered the lead project in this disease area (DA), have just started dosing in pivotal phase 3 trials. Expected study readout in 3 years, and a first launch in the first half of 2024.

2. Lavender which has started Proof of principle (Ph2 trial) and with an expected phase 3 start late next year.

3. Thyme which has started Proof of principle (Ph2 trial) and with an expected phase 3 start late next year.

4. Saffron which has started Proof of principle (Ph2 trial) and with an expected phase 3 start late next year.

In the table below we see the development and early market assumptions that were used to create the baseline portfolio. Ranges are indicated in some cases, and this is because we were uncertain about the quantity in question and did not want to specify single numbers.

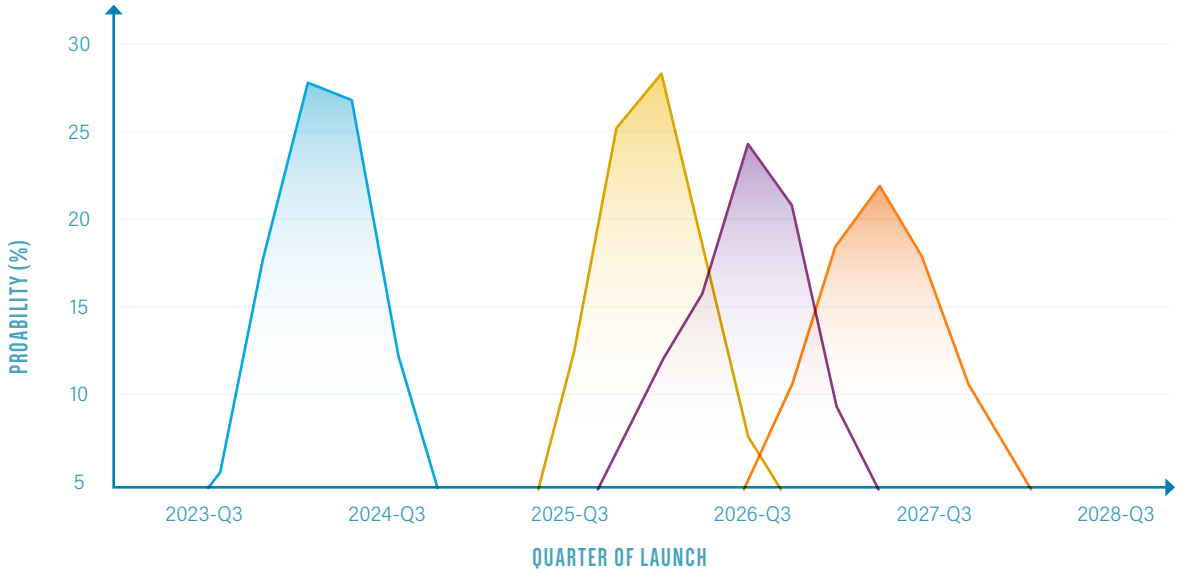
Here's a tip: Capture project timelines and costs using ranges instead of fixed numbers; The project team will be more comfortable, the number will be easier to believe, and they will provide a forecast that is richer in detail and better for making decisions.

PROJECTS		DURATION				COST				PROBABILITY OF SUCCESS				MARKET ASSUMPTIONS		
Project name	Current Phase	Ph1	Ph2	Ph3	Reg	Ph1	Ph2	Ph3	Reg	Ph1	Ph2	Ph3	Reg	Sales Ramp	Peak year sales	Loss of exclusivity
Caper	PH3			1.2	1-1.5			180-220	5-10			0.65	0.9	4-5	500-2400	2028.3
Lavender	PH2		1.9	2.5-3.5	1-1.5		40-60	150-200	5-10	0.35	0.65	0.9		2-4	500-600	2032.8
Saffron	PH1	0.4	1.5-2.5	2.5-3.5	1-1.5	5-10	25-60	150-200	5-10	0.6	0.35	0.65	0.9	1-3	400-800	2035.4
Thyme	PH1	1.25	1.5-2.5	2.5-3.5	1-1.5	5-10	25-60	150-200	5-10	0.6	0.35	0.65	0.9	2-4	400-800	2037.1

LAUNCH PROBABILITIES

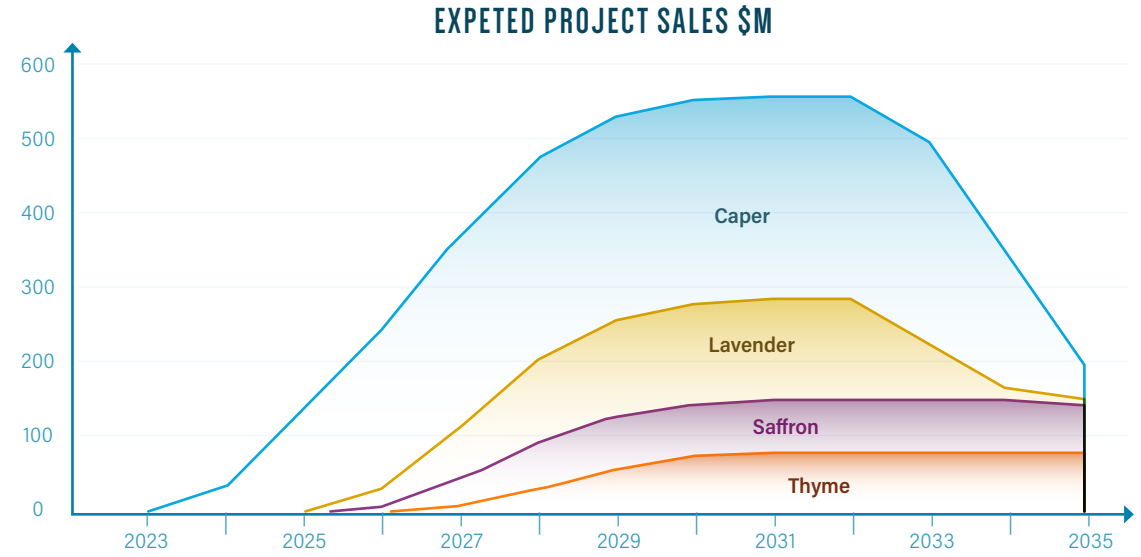
Since we are using ranges instead of setting up fixed milestone dates, the launch profile for this portfolio is somewhat - uncertain.

In the picture on the right you can see the launch windows for the assets in the portfolio. *Caper* will launch first, followed by *Lavender*, Saffron and *Thyme*. By the end of 2027 all projects will be either launched or terminated.

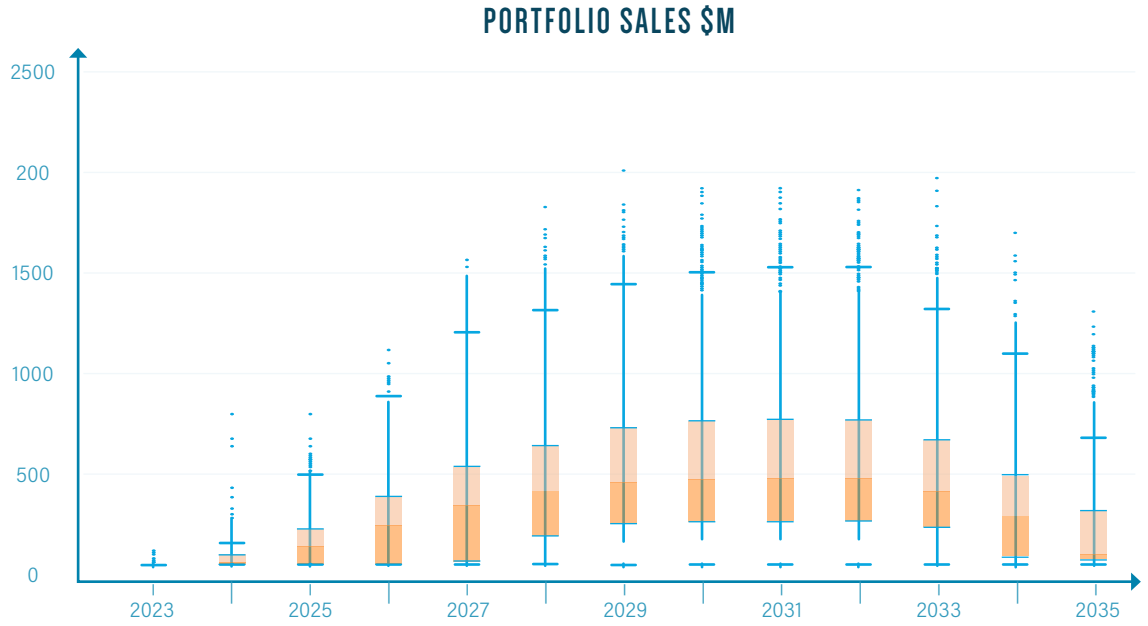


SALES IMPACT

What do these launch probabilities and launch windows mean in terms of future sales? The chart on the right shows expected sales for each one of the projects in the portfolio stacked on top of each other. These forecasts are risk adjusted, i.e., they include the risk of project failure. This means that the sales that we will se from the portfolio will never be as in the upper chart; Any project that launches will have larger sales than indicated by its color, but on the portfolio level we can expect a peak sales of around $550M.

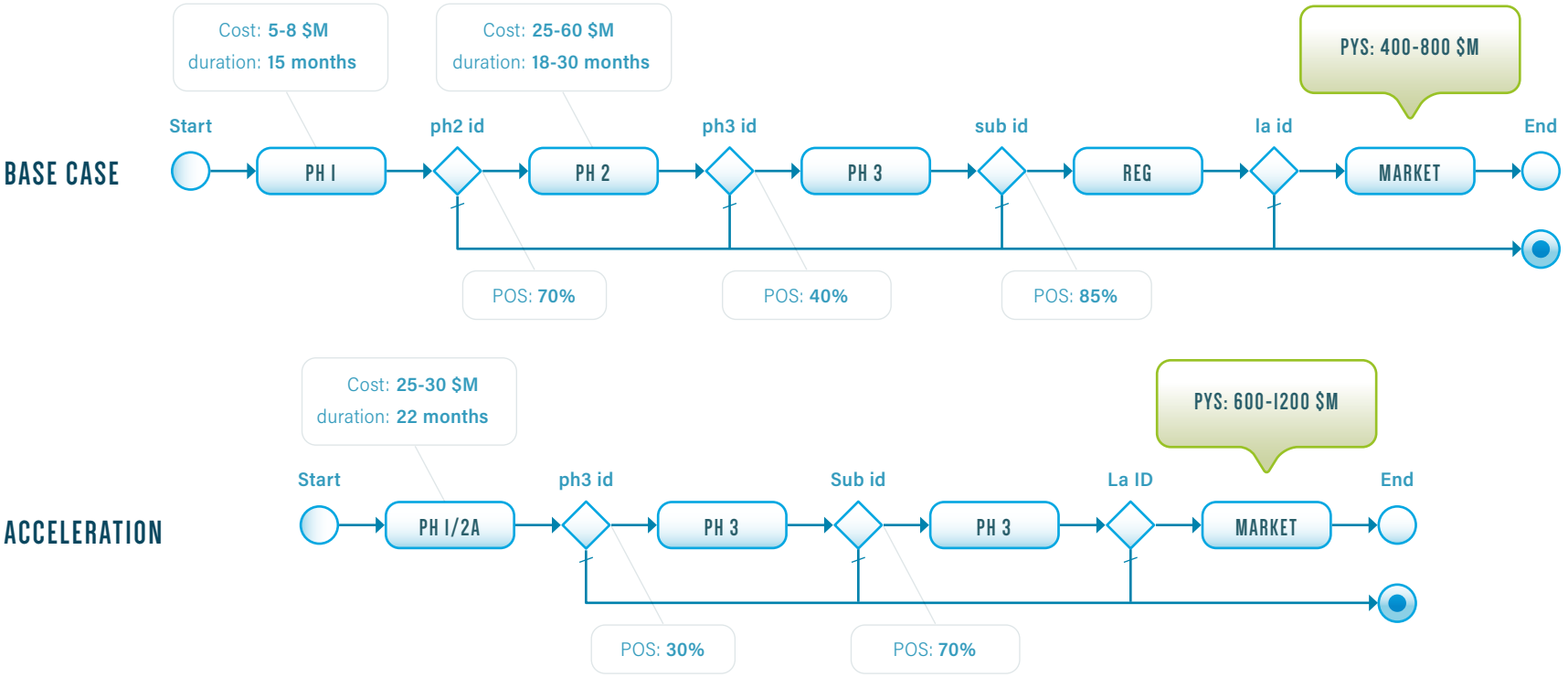


This is confirmed by the bottom box-whisker plot of the portfolio sales. The boxes indicates a 50% confidence range, and the whiskers a 90% range. If several of the projects are launched, we can expect sales in the upper range and if we launch fewer we can expect sales in the lower range. This is a great way of showing the uncertainty in potential outcomes for the portfolio and is more reliable as decision support material since it shows a richer view of potential outcomes.



Now that we have an understanding of the baseline portfolio we can start to look at strategies to improve portfolio cost, timelines and value. One alternative could be to accelerate projects so that is our first scenario »

SCENARIO I » PROJECT ACCELERATION

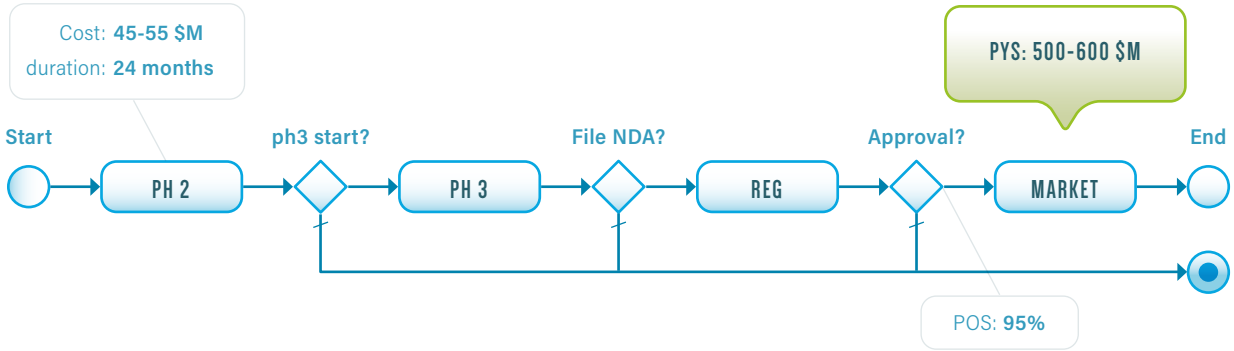


For the projects *Thyme* and *Lavender*, it is possible to change the structure of the program and accelerate development hoping for an earlier launch. In *Thyme*, the base case assumes a traditional development plan. We wanted to test a different strategy where we run a combined phase 1/2A, and then move directly into phase 3 if results are good enough. This will save a lot of time to launch and we believed that an early launch would give us a longer sales period while also increasing the market share. This is represented by increasing the range for peak year sales. Remember, this is a first overview of potential new strategies, so we are keeping things simple.

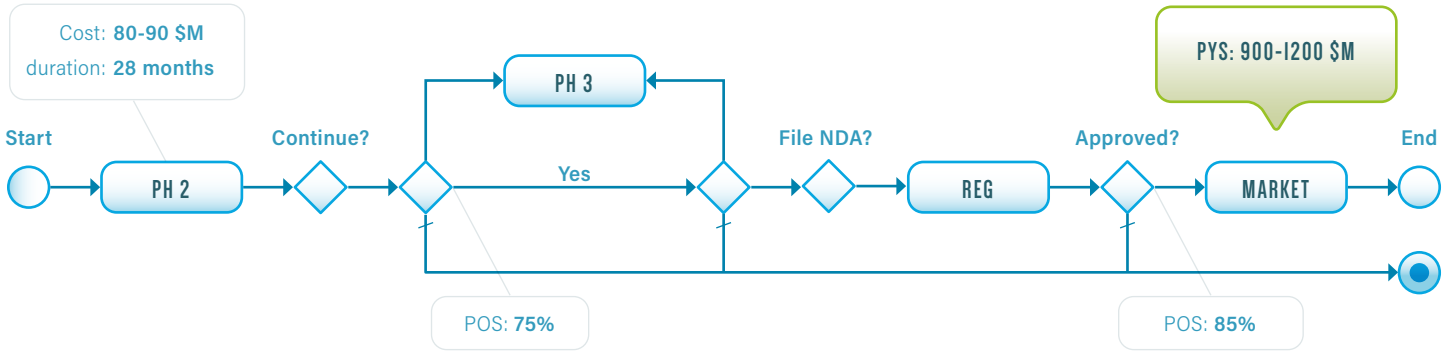
I used Captario SUM® to model the two strategies for *Thyme*, first creating the base case model and then creating the accelerated scenario as a copy of the first (picture above). Let's now focus in on the numbers. Costs to phase 3 will be about 10 million less if we go for the accelerated option, and we will reach ph3 at least a year faster. This speed comes with a greater risk of a phase 3 failure and more investment at risk along the entire project. Launching early gives us more patent protected sales, but there is also a potentially larger market share which is represented in the accelerated model by a higher peak year sales estimate.

For *Lavender*, the opportunity to accelerate is slightly different. By using a different end-point in phase 2 trials, the project may become eligible for fast track designation if the study results are good enough. Using the alternative endpoint will cost a lot more and take slightly longer, but will offer a significant chance to fast track the project - in this case that would mean filing after phase 2. In the picture below you can see how this was modeled using Captario SUM®. Again, I'll just point out some of the key points. In case of acceleration, we change the phase 2 studies, which will increase costs drastically for phase 2. This yields the possibility of fast tracking the project and filing after phase 2 if the results are good. However, this compound is still rather untested, and the risk of failure after phase 2 is 65%, regardless of which option we select, so the rate of investment at risk is very high if we choose the accelerated option. Even if we change the phase 2 to maximize the possibility to get a fast track status, we still run the risk of not seeing a result that is good enough to be eligible for fast track. In that case we would have no other option but to run a regular RCT phase 3 with pivotal trials. We have estimated this risk to 25% in the accelerated case.

BASE CASE



ACCELERATION



SCENARIO 2 » IN-LICENSING OPPORTUNITY

An alternative to accelerating our internal assets is to in-license. In a live case we would look at a number of potentials, but here we will only look at one project. The *Dill* project has just dosed in phase 2, and has an expected launch date in 2026. It has a great potential to become a blockbuster if all goes well. If added to the portfolio it will require substantial development investments for the next 5-6 years on top of any up-front payments and milestone costs. After identifying and creating the four scenarios, we will then analyze the differences from sales, cost, risk, and value perspectives.

SCENARIO SUMMARY

With our two improvement scenarios we have in practice four scenarios:

1. Base case

We continue with what we have. No additional investments in this portfolio.

2. Acceleration

We accelerate the two programs Thyme and Lavender, and keep the base cases for projects Caper and Saffron.

3. In-licensing

We aquire the asset Dill and develop this internally as part of this portfolio.

4. Acceleration + In-licensing

Perhaps we have the funding to do both?

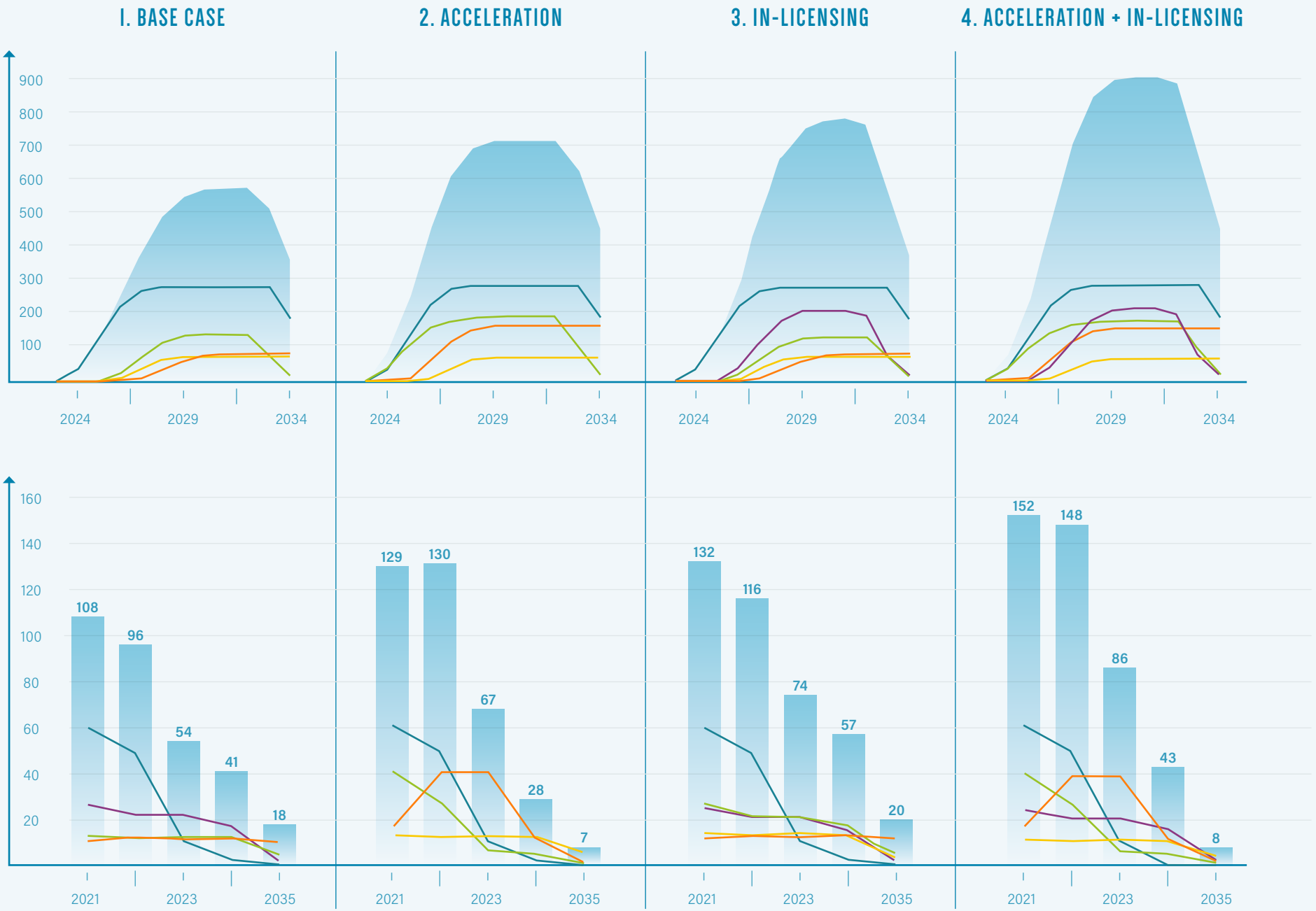
Graph 1: SALES (Top right)

The first blue area is the expected sales for the baseline portfolio which is - as we saw earlier - peaking at 550 MUSD/Year. If we accelerate development for two of the projects, we can see how the sales ramp up earlier and steeper than in the base case. Our peak is also higher because of the better market share. If we in-license, we can see that the peak is higher, but sales increase is slower than if we accelerate two of the programs. At a first glance it looks like the total risk-adjusted revenue will be better if we accelerate rather than license in.

Graph 2: COSTS (bottom right)

In terms of costs, we need an investment of $200M to cover the base case for the next two years. If we accelerate we will need 260M which is a 30% increase in budget. Since our peak sales go from 550 to 700, and we also add a year of peak sales, this looks like a good investment. For the in-licensing option, we would need a little less in the first two years, but more during the next three year. The increase in revenue though is slightly less. Based on budget concerns the two options are equivalent.

On the next spread we will look at portfolio value in terms of NPV →

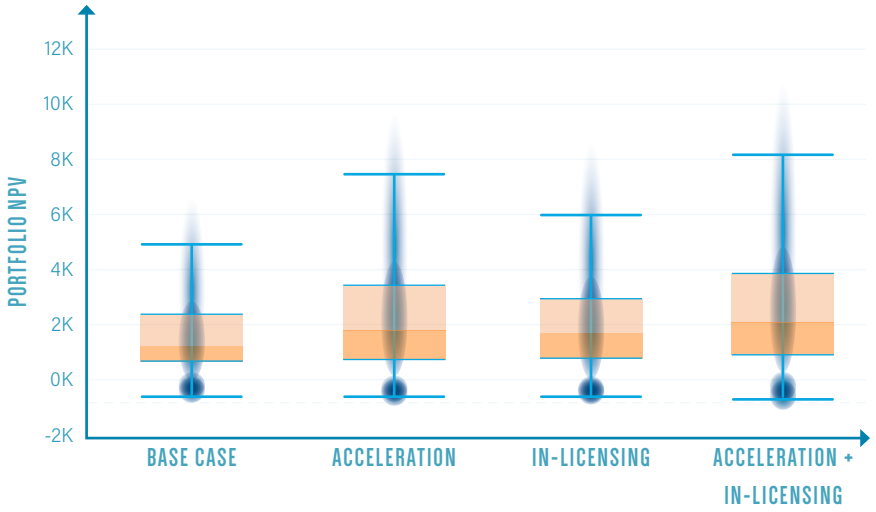

1. BASE CASE
2. ACCELERATION
3. IN-LICENSING
4. ACCELERATION + IN-LICENSING
900
800
700
600
500
400
300
200
100
2024
2029
2034
160
140
120
100
80
60
40
20
108
96
54
41
18
129
130
67
28
7
132
116
74
57
20
152
148
86
43
8
2021
2023
2035

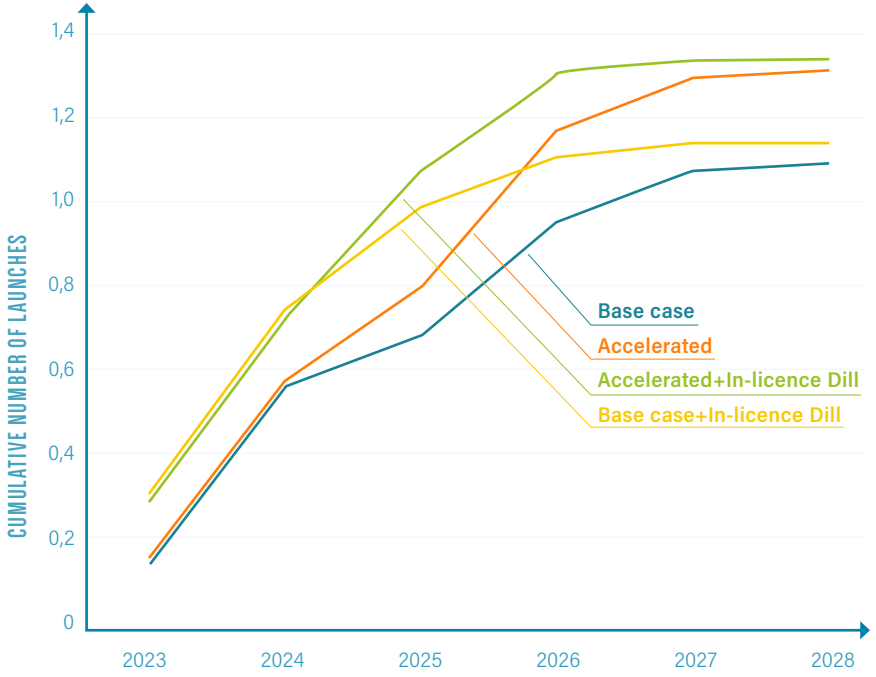
SCENARIO 2 » PORTFOLIO VALUE

In the top right graph we can see the spread of potential portfolio value based on the uncertainty in the portfolio models. Attrition is of course the major contributor to this uncertainty, but also things like time to launch, Peak Sales, and route to launch for the individual assets will affect the portfolio NPV. The eNPV is about $1.7Bn regardless of if we in-license or accelerate, but there could be more to learn from this data. If we just look at the negative NPV values, we can see that in the base case, the risk of loss (i.e., risk of negative NPV) is 23%. For the accelerated scenario this is about the same, but if we in-license this drops to about 17%. The reason is that we get more shots on goal if we in-license. In a portfolio of 4-5 projects, the risk of getting no launches is still quite large. If we add projects with positive NPV this risk is mitigated to some extent.

So, the perspective of risk-mitigation is also something to keep in mind when considering disease area strategies quantitatively.

Adding new independent assets into the portfolio will give us a better chance of launching products from the portfolio. If we accelerate, we only increase the likelihood of an early launch. This is illustrated in the line graph (lower right) which shows cumulative expected launches that the portfolio will generate.





SUMMARY

Here are my takeaway points from working with the quantitative aspects of disease area strategies:

1. Use ranges or functions to represent uncertainty in modeling assumptions, for instance to assess time, cost or sales. Drug development is risky, and we need to represent that risk in our models.

2. Since we are using uncertainty in the input, we will get uncertainty in the output. We need to make sure that the visualizations we use can illustrate the richness in the data, and that they can also use ranges.

3. When analyzing data, really dig into the details! In my experience, this is where the key differentiating factors are often found.

4. Compare options from many different perspectives! Look at cost, revenue, opportunities, risks , sales projections from many angles and use multiple visualizations to look at each data point

5. When creating decision support material, be sure to include the key factors that will influence an outcome the most. Tornado and scatter plots are good for this.

Quantitative analysis can greatly help decision makers understand the dynamics and possible outcomes of decisions. However, it does not provide definite answers. That is always up to the decision makers themselves!

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