PROJECT CASE STUDY

NDA SUBMISSION STRATEGY

BY MAGNUS YTTERSTAD

CAPTARIO

BACKGROUND

A while ago I was engaged in a client project where we developed the launch strategy for a compound targeted for multiple indications.

The compound had just started phase 3 trials in two indications. In this case, only one NDA process is allowed at any given time and this meant that we would have to choose between two options regarding how to file for approval:

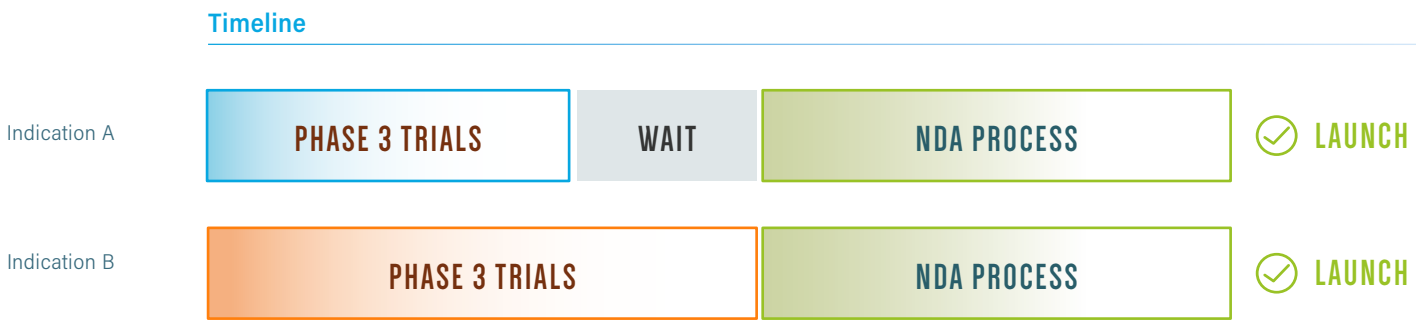
1.PARALLEL FILING

After the first phase 3 trial we wait until the trial in Indication B is also completed and then file an NDA for both indications. This would mean that, if successful, both indications will likely get approval at the same time but with the cost of a delay for indication A.

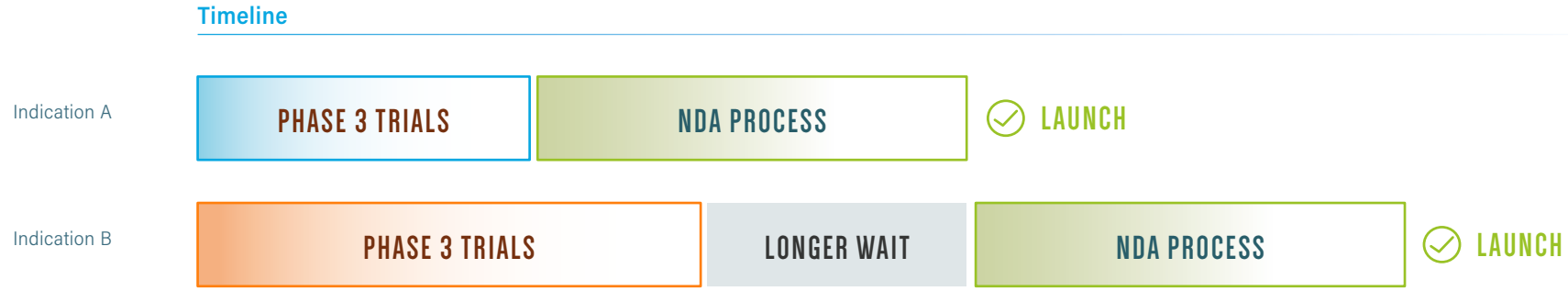
2.SEQUENTIAL FILING

After the first trial, we file the NDA for that indication. When the trial in the second indication is completed, we will wait for the first NDA process to finish before filing the second. This scenario would mean indication A is launched as early as possible, but at the expense of time to launch for indication B.

SCENARIO 1 PARALLEL FILING



SCENARIO 2 SEQUENTIAL FILING



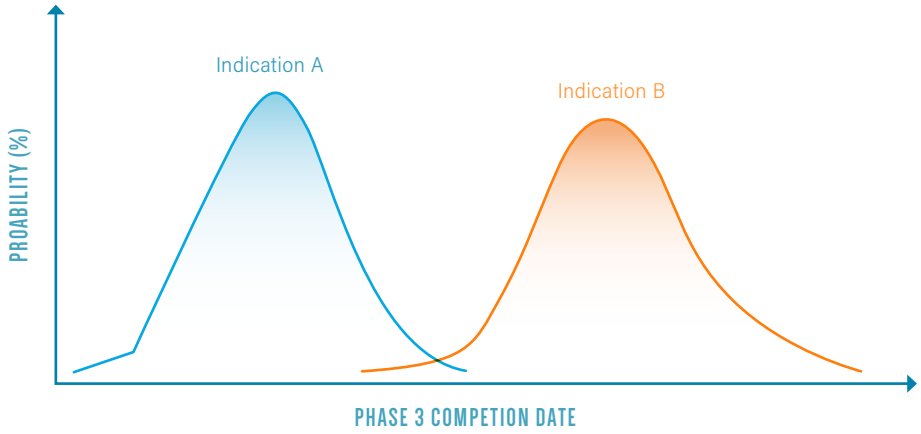
So the big question then was to figure out which option gives us the best outcome. But there were a number of complicating factors that we had to take into account when modeling these scenarios. And as we will see, these factors makes this a bit more complicated than the picture above has lead us to believe.

PROJECT EVALUATION MODEL DYNAMICS

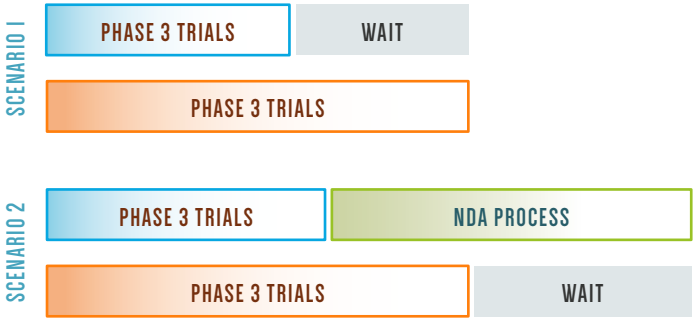
If all the facts about the projects are known, it should be easy enough to just find out how long the wait periods are, find the launch dates, and then calculate revenue for each scenario. Then, from that, calculate eNPV, ROI, or whatever value metric you want to use! Easy enough, right? Well, not really!

As we all know, there is no such thing as a fixed timeline for a phase 3 clinical study! A hundred things can happen that will invalidate the plan and cause a delay. So instead of setting fixed dates in the models for when the studies are done, we use probability distributions that represents the time to complete the phase 3 trials for indications A and B.

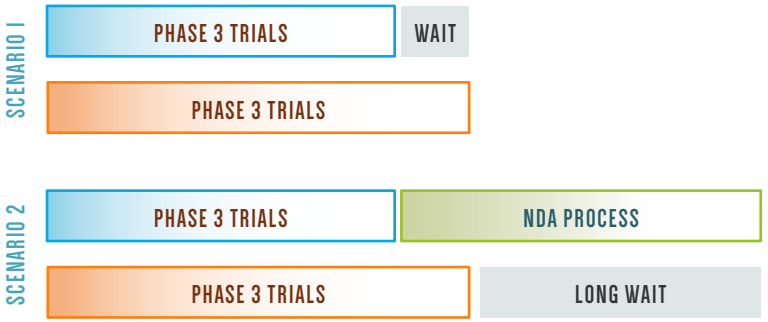
In the line graph (below) we can see that the time difference can be next to nothing or can be quite long, and this difference in timing has a considerable effect downstream for the two scenarios:



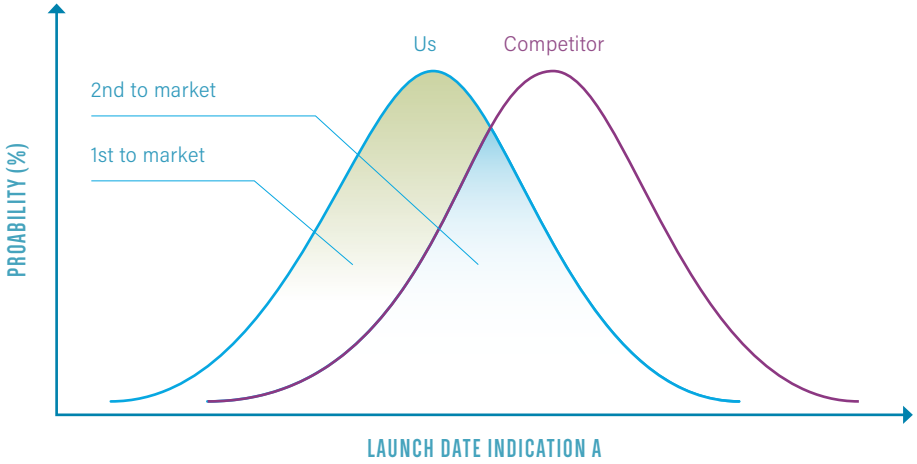
A long time difference means that the wait period for scenario 1 is long, and the wait period for scenario 2 is shorter:



A short time difference between the studies will lead to a short wait period for scenario 1, but a long wait period for scenario 2:



To further complicate matters, there is a competitive situation in Indication A. If we launch first, we will secure a majority of the market. If we don't launch first, our market share will be much less. The market models for these projects are dynamic in a lot of ways, most importantly in that they don't assume a particular order of entry - that will play out as a result of running simulations. The use of probability distributions to represent time for activities will give us a launch time which is also a window. We then use our CI information to create a similar launch window for the competitor.

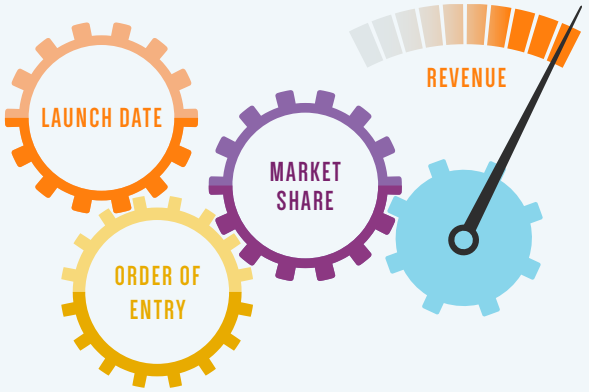


The graph above shows launch for Indication A and the competitor. It also has order of entry marked by the colored areas. The size of the green and blue fields roughly indicates the likelihood to be first or second to market given that both projects launch.

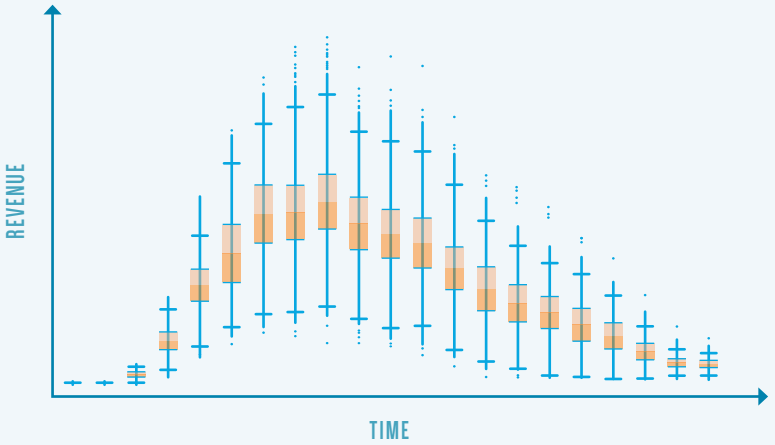
Now here comes the interesting part: Under scenario 1 (detailed on page 3) we will wait for the second trial to complete, which delays the filing date for indication A. This will push the blue curve (above) to the right which will make the green area smaller and the light blue area larger. The longer we wait, the less chance we will have of being first to market! We use this dynamic in the model to evaluate the project.

REVENUE IMPACTS

The revenue model uses launch date (and competitor assumptions) to find out the likelihood to be first or second to market, which in turn determines the size of the market share, which then has an impact on the forecast revenue.



Other factors that impact revenue are the launch date itself, as well as patient volume and price. All of these are represented by ranges of values, and all together they help us form sales forecasts that includes ranges rather than fixed point estimates.

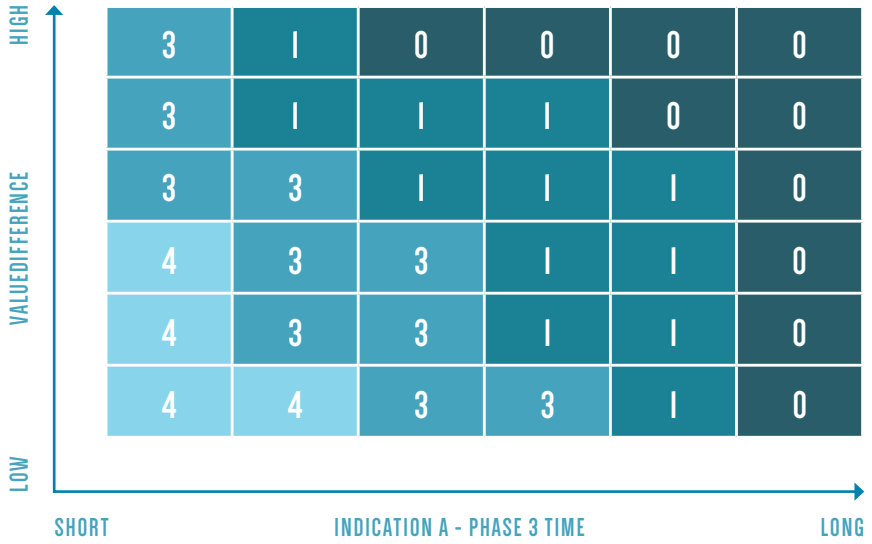


CONCLUSIONS

After building up the models we ran simulations where we evaluated the two scenarios.

We evaluated each project by itself and also looked at the effect for the entire program, i.e., the value proposition for both indications. If you recall, our task was to find out if we should wait for the second trial to complete before filing, or if we should file the two indications sequentially.

We realized that there are two major factors that influence this question. The first factor is the timing of the first trial to complete. If it finishes early, we can wait longer for the second indication and still have a reasonably good chance of being first to market in Indication A. The second factor is the difference in sales potential between the two indications. If Indication A is 4 times as valuable as Indication B, then we should not wait as long as if they are more equal in value.



This newfound knowledge, together with the quantitative data, allowed us to create a number of analytics to support this decision. For instance, we created a heat-map (above) that indicates the max number of months to wait for Indication B before filing, depending on when the first study was done.

SUMMARY

We used Captario SUM® to create the models, run simulations, and analyze results throughout this engagement and I am happy to say that we were quite successful in meeting client expectations. Here are some key modeling concepts we used when building the model. These are essential and should be available in your project and portfolio modeling solution:

1. Use ranges or functions to represent project uncertainties, for instance when estimating the duration or cost of clinical studies. If you are limited to using point estimates, you will create a plan rather than a forecast. A plan is an idealized idea about what you want to happen, it says little about what could happen.

2. Combine a dynamic market model with the R&D model. You should be able to use output from R&D such as launch date to influence the sales modeling. If we launch late, our sales window will be smaller. Also, as in this case, our sales model should have the flexibility to include competitors, price and patient volume variations and so on.

3. Just as we use uncertainty in the input, we should be able to illustrate uncertainty in the output as well. The revenue chart earlier in this article is an example of this. Box-Whisker and scatter plots are invaluable to understand patterns and how project parameters interact and affect output variables such as sales, launch date or project value.

CAPTARIO

CAPTURE YOUR FUTURE

Captario SUM® is one seamless solution for project and portfolio analysis and decision making. If you would like to learn more, reach out to us at team@captario.com

EU Captario AB, Storgatan 53,
411 38 Gothenburg, Sweden

team@captario.com
www.captario.com