PROJECT CASE STUDY

EVALUATING FAST TRACK OPPORTUNITIES

CAPTARIO

BACKGROUND

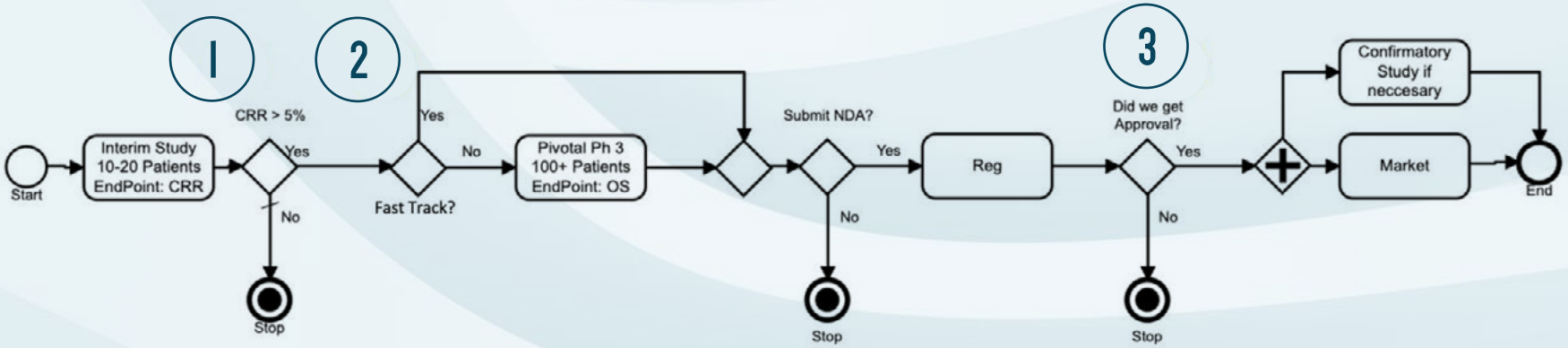
Over the past eighteen months we have participated in efforts to develop product strategies for a number of oncology assets.

These development projects, which are run by different companies, have had a couple of things in common:

- **They are in early clinical testing with little or no clinical data**
- **They have a potential to be granted fast track designation by FDA**
- **There is a complex market situation with several competitors within and outside of the class**
- **In this article I will show an example of how to use quantitative analytics to evaluate potential fast track opportunities**

CASE STUDY PROJECT

We will use an example project in this article, and I will start by going through how to build the model using Captario SUM®. The picture below shows a process map which is the foundation for the model. It describes the high level activities and decisions we will go through in the project.



A PLAY-BY-PLAY OF THE STRATEGY

1. The first step is to run a small study with very few patients (represented by the first rectangle in the process map); We have seen as few as 5-15 patients for rare indications. In many cases this study is using a surrogate endpoint. For example, if the registration endpoint is Overall Survival, the surrogate endpoint could be Complete Response Rate - CRR. Based on data from the trial a decision is made to continue development or stop - typically if the patients in the study show no or very little response to the treatment. In this case, if less than 5% of patients are complete responders, the program is stopped. We create this dynamic with a model of the clinical effect of the drug.

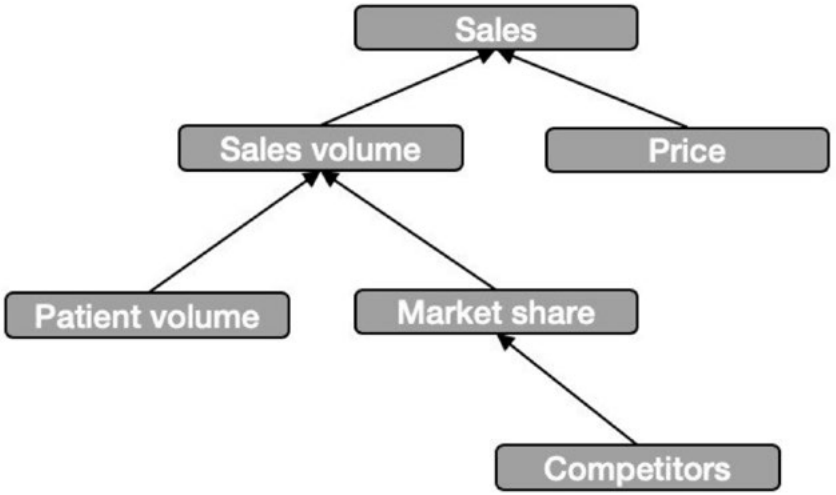
2. The second decision is also data driven - if we have exceptional response rate from the first study, for instance a CRR of above 35%, we may be eligible for fast track designation. If so, we will go straight for an accelerated approval and run a confirmatory trial later. If we do not see an exceptional result, we still have the option to run a pivotal phase 3 trial to investigate the effect on the primary endpoint.

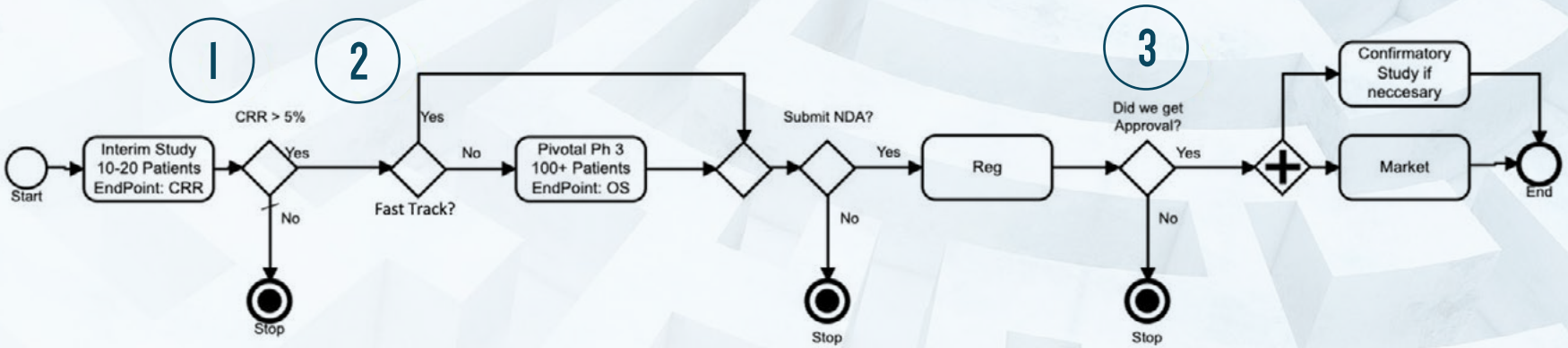
3. Regardless of development path (fast track or not) we will hopefully get an approval in the end. Post launch we will try to maximize the return on our investment and in modeling terms this is managed by a sales model.

MODELING SALES

The sales model has to be dynamic enough to handle the fact that we can have different launch windows depending on our development path.

We have found the following useful when building sales models for fast track opportunities: Sales is a function of Sales Volume and Price. Sales volume on the other hand is dependent on the Patient Volume and Marketshare. Marketshare in turn is dependent on the competitive situation. We use order of entry and number of entries to determine market share. Of course this can change depending on the situation.





We have now captured the base case project which includes a small phase 2 study and a pivotal Phase 3. The huge upside of fast track designation is also covered; If we see an exceptional result in phase 2, we will omit the pivotal trial and go directly for an accelerated approval. After registration, the market model uses launch date as an input to differentiate between launch timings of the two paths. This is reflected in the order of entry, which determines market share. If we launch early, we are more likely to be first to market, which gives us a higher market share. That is how the dynamic works in reality, and that is how we are modeling it!

Once the development and sales models are built we populate them with assumptions. All the studies will have cost and time assumptions, and the likelihood of success is derived from the effect modeling that was mentioned earlier. Some assumptions are single values, but most are specified as ranges to reflect the uncertainty of drug development.

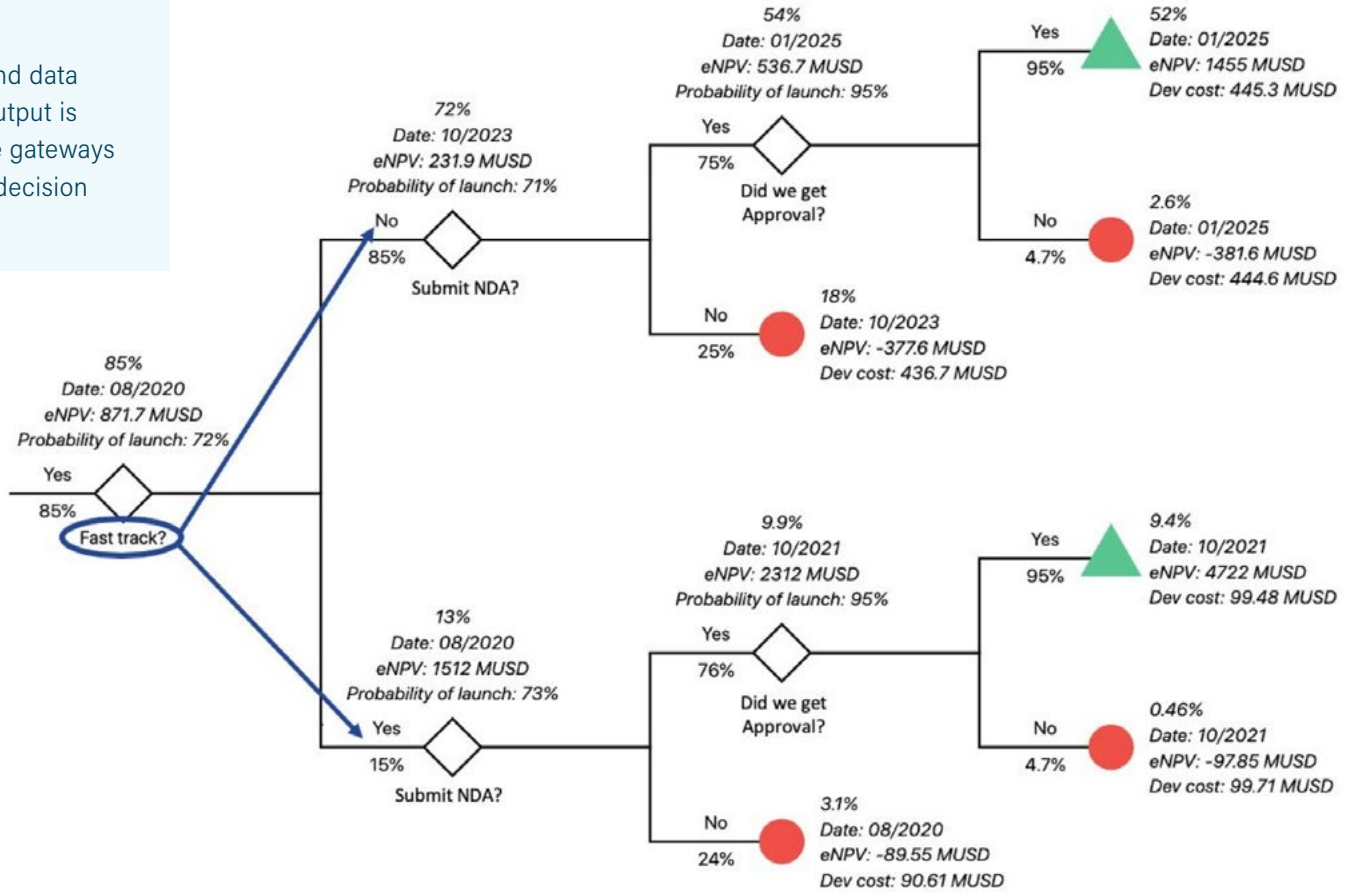
After populating the model we run Monte-Carlo simulations to generate a huge amount of outcomes for this project. In the next step, we will go through some of the analyses we can use to determine project value.

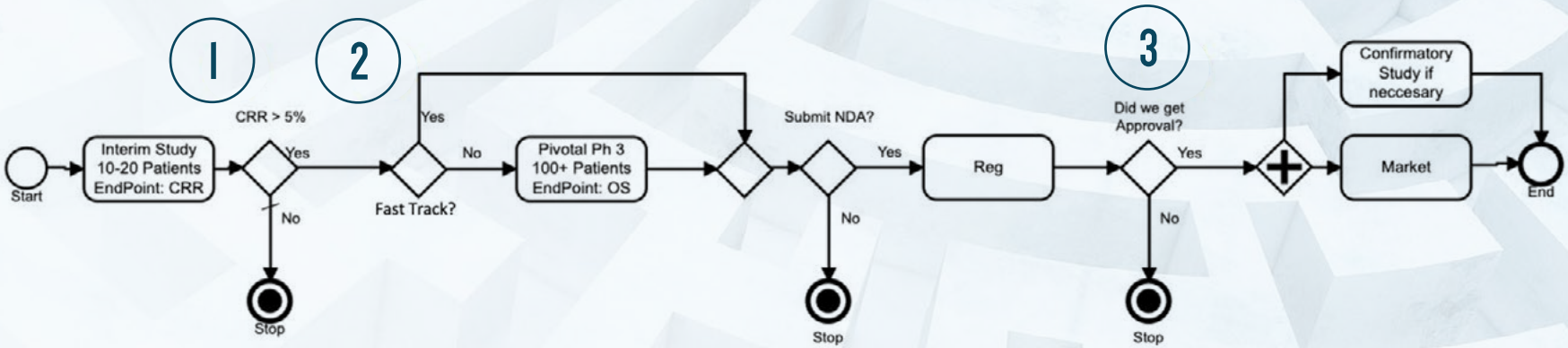
UNDERSTANDING PIVOTAL DECISION POINTS

We run Monte-Carlo simulations to generate a huge amount of outcomes for the project represented by the model, and we then analyze that data.

THE DECISION TREE

We use charts and graphs to understand data and to find patterns. One very useful output is the decision tree, which focuses on the gateways in the model which represents pivotal decision points or outcomes.





INSIGHTS

The decision tree (left) outlines our three most important decisions:

- **Did we get the fast track?**
- **Did we submit?**
- **Did we Launch?**

Each one of these match a gateway in the process map (above), and for each one we can easily assess what a yes or no means in quantitative terms.

First we can see that that the likelihood of getting fast track status is about 15%. The value is almost doubled, from $871M - which is the current value of the project - to $1.5B.

If we follow the other path we can see that the value drops to $232M, which is an effect of definitely loosing possibility of fast-tracking.

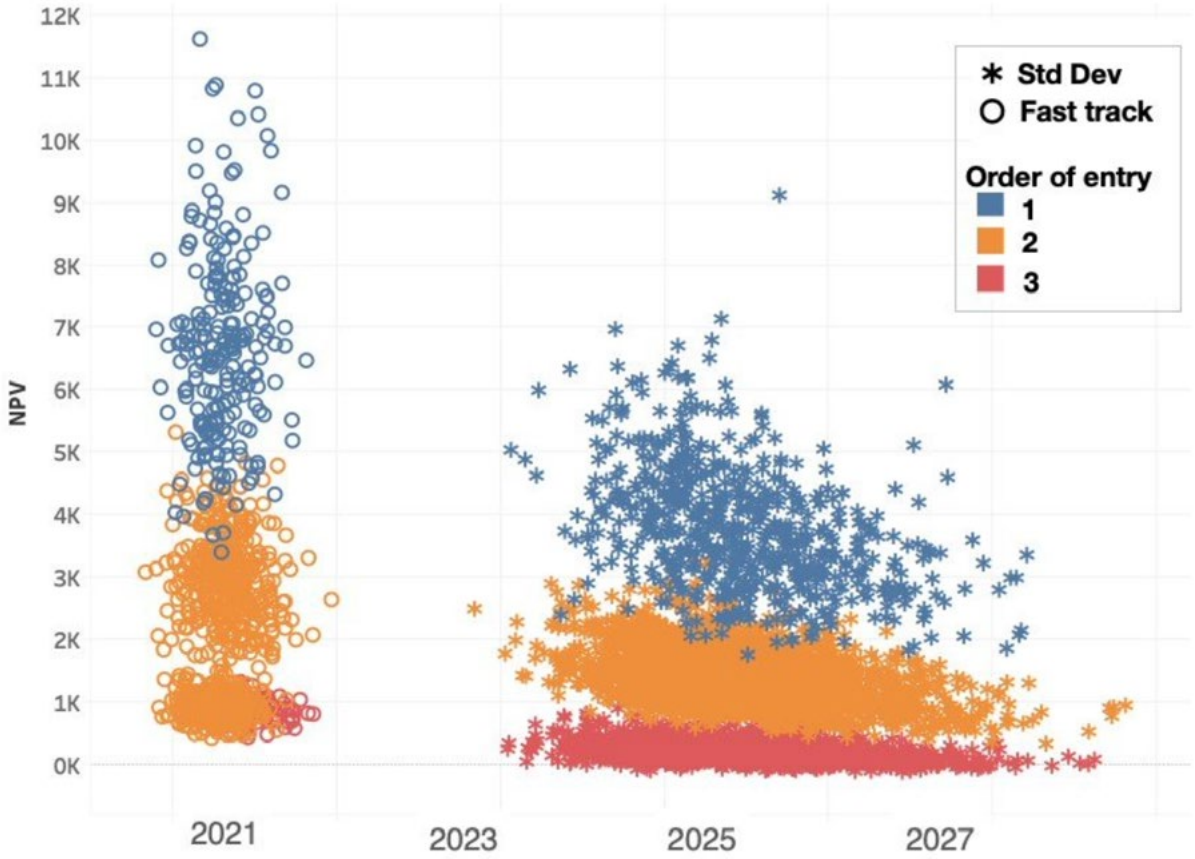
The red dots tells us about the risks and the green triangles show us the upsides and ROI if we launch. Comparing the potential paths to launch is a very good way of getting an overview of the risk and value of the project.

UNDERSTANDING VALUE DRIVERS

The next thing to look at are value drivers. I like scatter plots because they both give an overview and can reveal interesting outliers.

This chart shows Launch Date on one axis and NPV on the other. We can see that our launch timing is highly dependent on if we get the fast track, although that does not explain the variation in launch timing for standard development path. We may have to dig deeper to find our what causes that variation.

The color indicates if we are first, second or third to the market. This seems to have a big influence on the value of the project, but again, does not explain the entire variation. We may need to dig a bit deeper to fully explain the variability in project value.



SUMMARY

In this article we have tried to show one approach to modeling and evaluating drug development projects with a fast track upside. The next step after getting to this point would be to continue to work with the model to find better compromise between time and cost so that the value - all things considered - is optimized. This is a highly iterative process that requires involvement from several members of the project team.

There are a number of modeling capabilities that are must-haves for this level of realism in strategic decision support:

1. Clearly, getting fast track designation and launching early is a huge upside for the project, and it is fundamentally important that we can capture alternative paths to launch in the model and subsequently allow them to impact the project or strategy value.

2. The sales model must be dynamic enough to take into account which path has been taken to get to a launch. If we launch 2-3 years early, that should have down-stream effects on order of entry and sales in the end. So rather than providing a simple sales curve, the sales model should be a function of R&D outcomes and take into account the competitors and other market factors.

3. If there is uncertainty in the project, we must be able to represent it in the model. The model must allow ranges instead of single values.

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