Analysis of a Drug Candidate in Clinical Trials

DPL Case Study

Background

A mid-sized pharmaceutical company, General Biosciences (GB), has a drug candidate compound in Phase 1 clinical trials. GB wants to know the value of the compound, its chance of reaching the market, and how much revenue the drug would generate if approved.

The compound's primary indication is for a chronic and relatively common condition, so its market potential is high. However, the target therapeutic area is crowded and competitive. Several "first generation" drugs already treat the condition, so GB's drug will have to offer a distinct advantage. While GB believes the drug would fit well within its portfolio of marketed products, the estimated cost of development is large relative to GB's earnings. If the risk is deemed to be too great, GB may seek a partnership with another company.

Clinical Development Risk

Like any drug, GB's compound must clear a number of technical and regulatory hurdles before it can be marketed. GB's analysis team took the traditional phased approach to modelling the risk of development failure. For each of the three clinical development phases, a probability of success was estimated based on historical failure rates and the specific risk characteristics of the compound.

For Phase 2, success was separated into two scenarios. Phase 2 dose finding studies will reveal whether the drug needs to be administered once or twice per day. Because patients might take the drug for years, this convenience attribute is critical to success in the market. The phases of development, from Phase 1 through Regulatory Approval, can be seen in the Decision Tree in **Figure 1**.

Revenue Forecast

Many factors influence the revenue GB will earn if the drug is approved and launched. The analysis team started by defining scenarios for the overall size of the market for drugs in the class. Another key factor was the price level that GB would be able to negotiate with health care authorities in major markets.

Market share was highly uncertain because many factors in the drug's overall profile were still unknown. The team decided to use three scenarios for market share, with probabilities depending on the outcome of the Phase 2 studies. These relationships can be seen in the Influence Diagram and in the Node Definition dialog box for Market Share (**Figure 2** right).

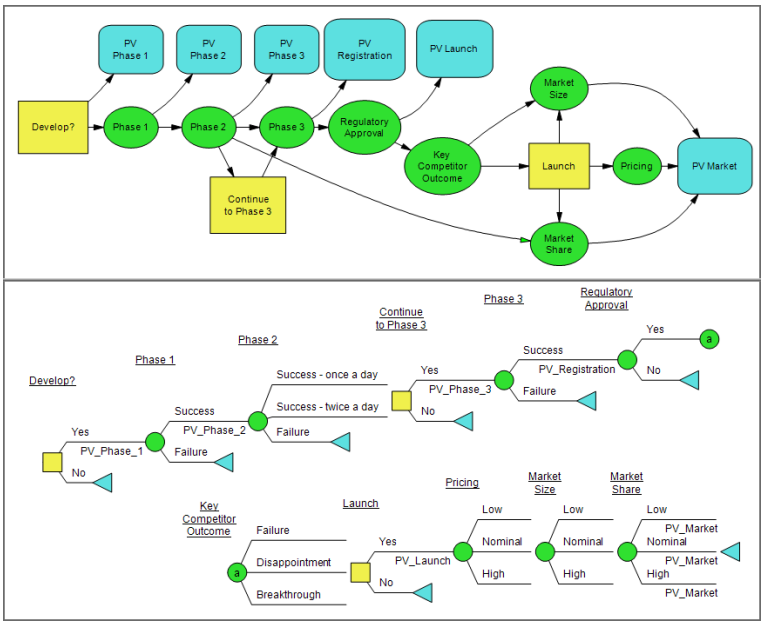

Figure 1. DPL™ Model – Influence Diagram and Decision Tree

Another key factor in the revenue forecast was the clinical success or failure of a key competitor. Unlike GB's compound, which was an incremental improvement on first generation treatments, this competing treatment could create a whole new drug class, dramatically shrinking the market for drugs in the old class. Fortunately for GB, this competitor faced significant hurdles to approval of its new breakthrough compound.

Optionality

GB knew it could stop the project at any time if the expected costs outweighed the expected benefits. The analysis team decided to consider two abandonment options: one before entering expensive Phase 3 trials, and another immediately before launch. Crucially, GB would be able to make the latter decision after knowing the key competitor's clinical results.

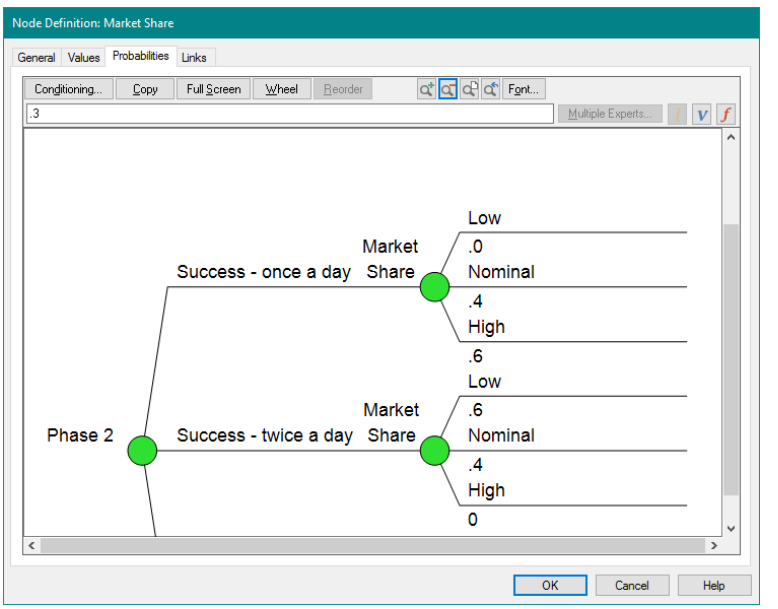

Figure 2. Conditional Probabilities for Market Share

Results

The expected net present value of the compound was approximately $11 million. The blue line in **Figure 3** shows the broad range of possible outcomes -- from losses of over $200 million to gains of over a billion.

The option to stop development before Phase 3 had a significant effect on value. Terminating the project is optimal when the Phase 2 outcome is the less desirable, twice-a-day regimen. Without the option to stop, the value of the compound would be only $7 million, reflecting the fact that many of the twice-a-day scenarios, while technically successful, are money losing. The risk profile for the compound assuming no flexibility is the red line in **Figure 3**.

The Policy Summary™ (**Figure 4**) shows that the decision to stop development before launch is never taken. This partly reflects the fact that the earlier option filters out many of the undesirable launch scenarios.

The Policy Tree™ (**Figure 5**) shows the costs, revenues and expected values in each possible path through the tree. The optimal decision policy for the Continue to Phase 3 decision is seen in the branches printed in bold -- Yes for Success once-a-day and No for Success twice-a-day.

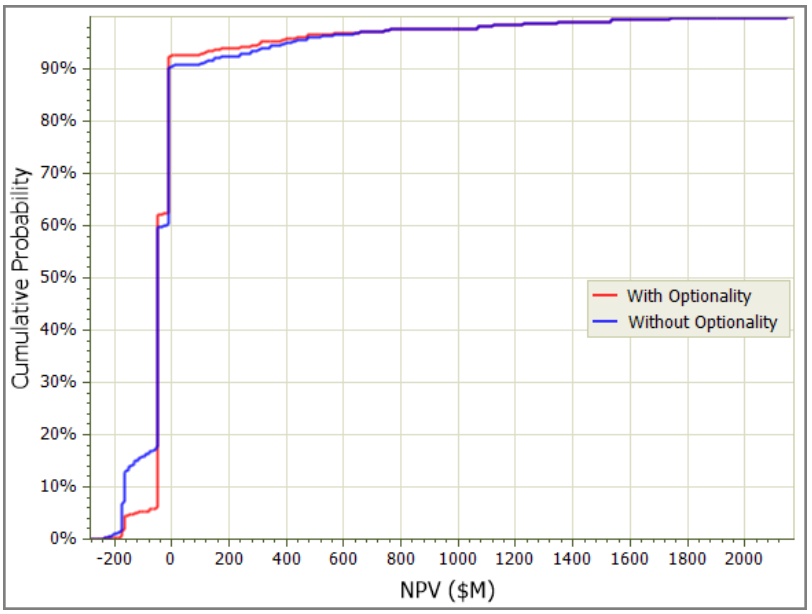

Figure 3. Risk Profiles with and without Optionality

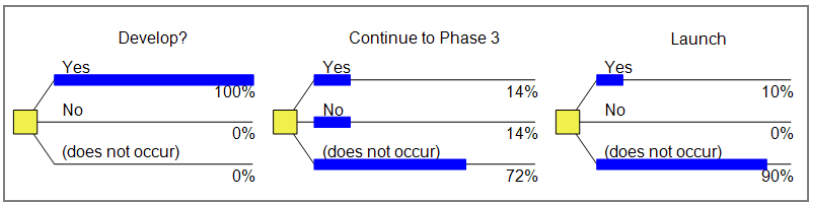

Figure 4. DPL Policy Summary ™

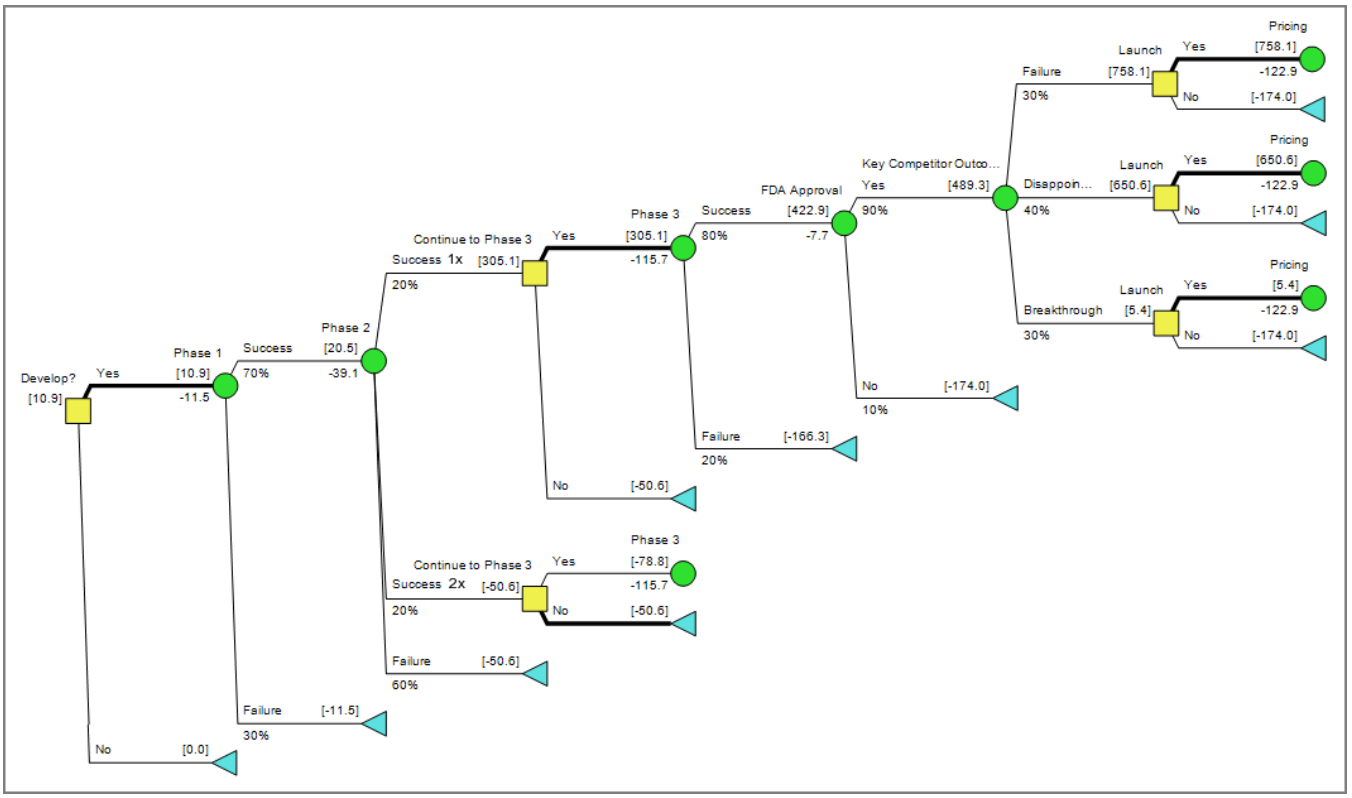

Figure 5. DPL Policy Tree™ output showing Optimal Decision Paths