Santen A Clear Vision For Life

Forecasting & Planning Tool

User Guide

Contents

WHY SHOULD I USE THIS TOOL?

The stated purpose of this Tool is to allow Project Managers and Global Program Leaders to make more efficient end informed decisions during planning and forecasting Meetings with their teams. To meet this purpose, this Tool will enable Planning Teams to:

1. *Learn to identify which development decisions are most impactful to an asset's value*
2. *Understand how those decisions impact that value or create further risk*
3. *Evaluate and communicate that asset value to/from other functions in the organization*

WHEN SHOULD I USE THIS TOOL?

The Tool is designed to be used in the context of a development planning team Meeting, both during early stage development (R2 / D1) and late stage development (D2 / D3). Please note that it is not intended for individual use, nor is it intended to replace any more accurate forecasting tools currently used by the Project or Portfolio teams. The Tool guides development teams through three phases of the Meeting: create greater alignment & intentionality during planning; generate insights regarding which development decisions are most important; and support commitment to action from the team following the Meeting.

Ultimately, it is the role of the Project Manager and Global Program Leader to guide the team through the Meeting's use of the Tool, and to hold team members accountable to outcomes following its use.

WHAT SHOULD I EXPECT AS OUTCOMES OF THE TOOL?

The Tool is action-oriented, as it will provide each team member with clarity of how their function's actions directly impact the value of the asset under development. Because of this, each team member will be responsible for taking at least one action after the Meeting and measuring the success of that action based upon its impact to the business.

While this action depends on the individual, there are five behaviors that this Tool promotes:

1. *More informed planning at each stage of asset development*
2. *Prioritization of investments and decisions based upon relative impact*
3. *Greater accountability for project risks and outcomes*
4. *More timely information and feedback to other stakeholders at Santen*
5. *Creation of reasonable scenarios and backup plans in the case of setbacks*

WHAT SHOULD I PROVIDE MY TEAM BEFORE THE MEETING?

In order to facilitate the planning stage at the beginning of the Tool's Meeting, each team member will complete individual pre-work in advance of the Meeting. This pre-work will inform each team member about the Tool and what he or she can expect to achieve by using the Tool. To send and process this pre-work, follow these four steps:

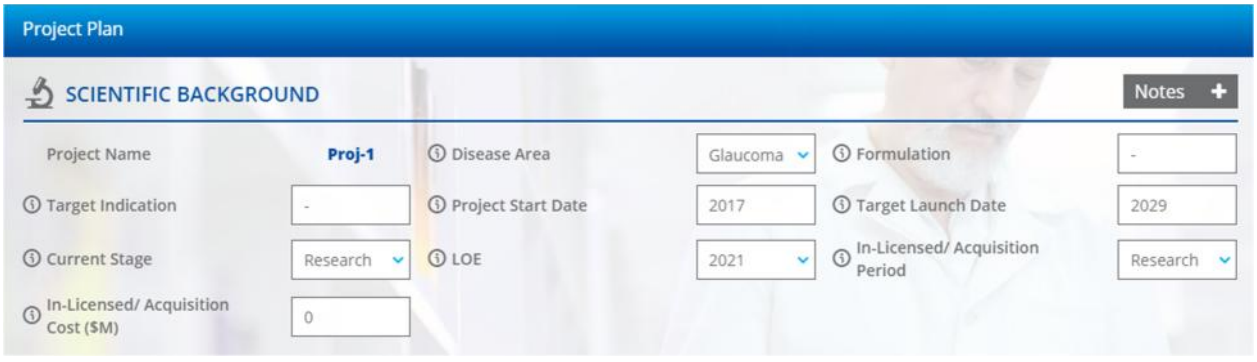
1. **3 weeks** before the Meeting, send each member a briefing* found here.
2. Allow each team member **1 week** to complete the briefing.
3. Each member sends you his or her briefing, so you understand the team's thinking.
4. As you begin the Meeting, use each of those briefings to inform the team's total plan.

***Note**: You, as the Meeting Leader, should determine which three metrics are most important at the beginning of the Briefing document. Fill these out before sending.*

HOW SHOULD I BEGIN MY MEETING? – *PLANNING STAGE*

How do I complete the asset's Scientific Background?

You will first define what you know about the Target Product Profile in the "Scientific Background" portion of the Tool's Planning Page. This area captures given information about the product, such as its *Disease Area* or *Acquisition Cost*, which will create a general baseline for the scenarios that you will construct. Please note, if a detail of the exact target profile is not available, choose the closest possible option.

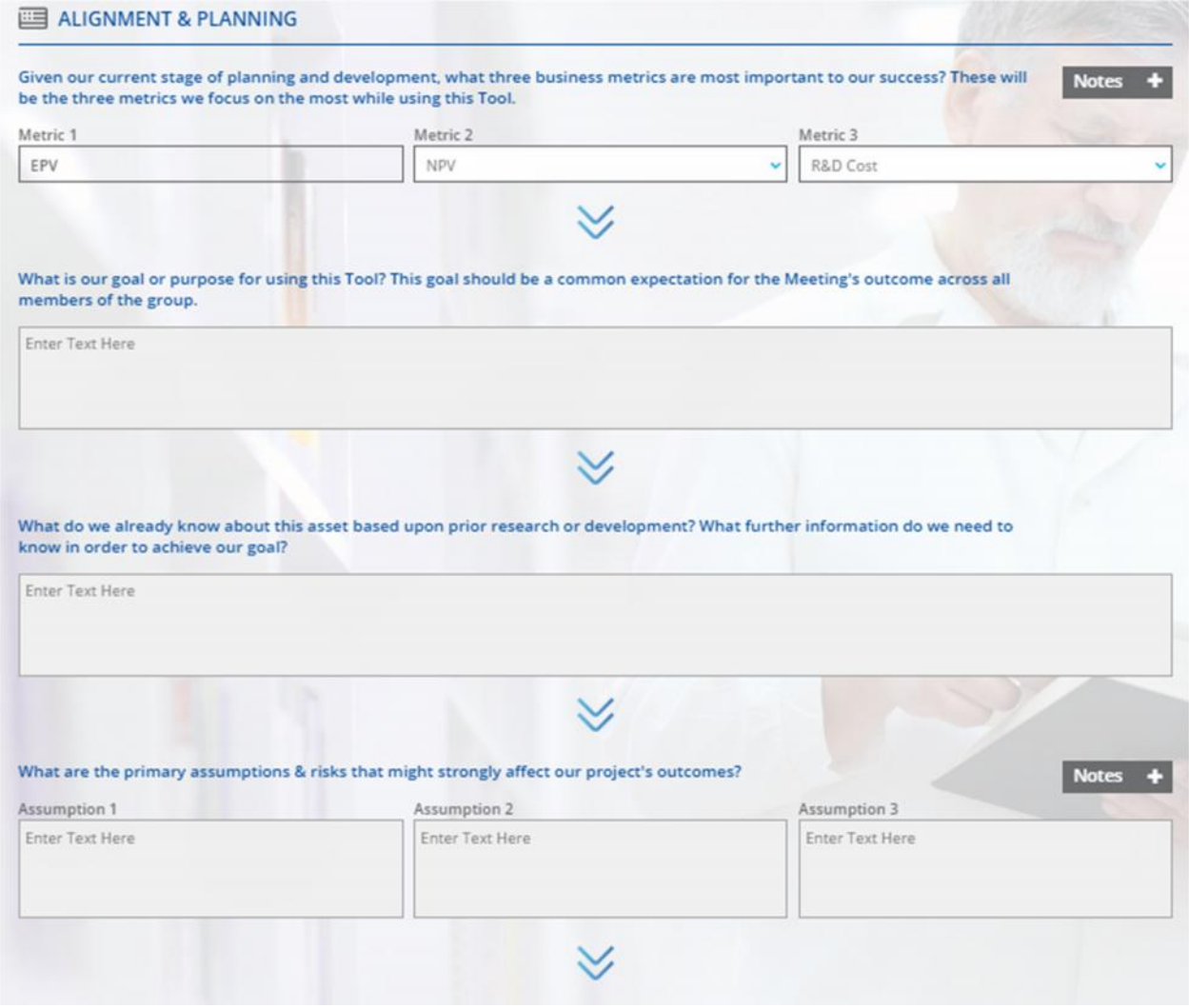


How do we answer the Alignment & Planning questions?

This area of the Tool appears identical to the pre-work briefing that each individual completed beforehand. The goal here is to create a *common* answer to each of the questions on this page. Where you focus your attention on the decisions within the Tool will depend on what the team believes to be most important here.

There are two important suggestions for efficiently completing each of these questions:

1. Where individual responses are similar, reduce time by entering their common response
2. Where individual responses are most different, spend more time to reach a compromise



How do I know when I am finished with my Planning Stage?

The Planning Stage acts as your hypothesis, which you will test across different scenarios involving product development decisions. Most important here is both that your team agrees upon each response and that each response has enough detail that you can act upon it. Do not move on to the Scenario Pages until you have filled in all three *Metrics* and all three *Assumptions* because you will come back to these decisions at the end.

HOW DO I TEST DIFFERENT SCENARIOS? – GENERATING INSIGHTS

Each of the scenario tabs will allow you to create a different development plan, beginning from R0 / R1 / R2 though the completion of D3. These plans will include both research & development decisions, as well as commercial and manufacturing decisions to construct the asset's market value.

How do I interpret my Dashboard?

At the top of every Scenario Page, you will find the three metrics that you chose during Alignment & Planning. These metrics will change in value as you change parameters and decisions below. Whenever you change or make any decision, note the effect on the Dashboard metrics. It is the best guide of how impactful each decision is on the asset's value.

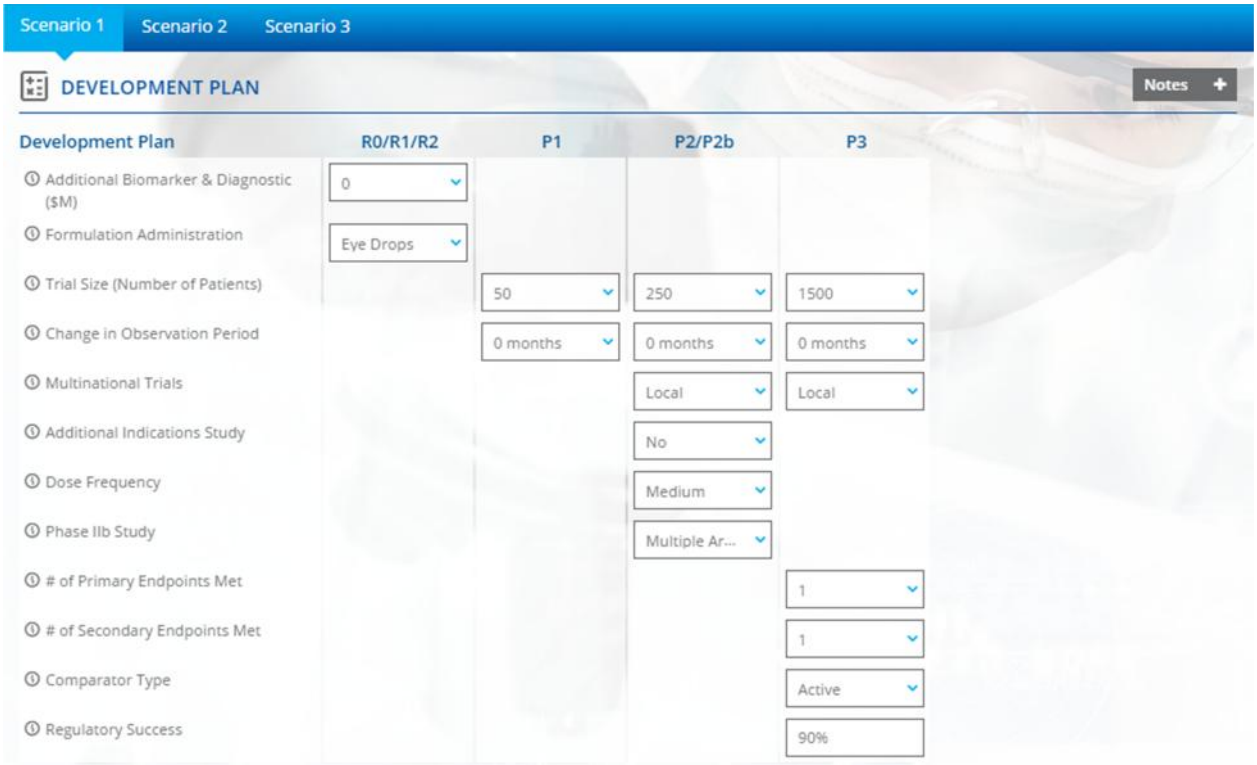
How do I complete Scenario 1 – Base Case?

While each Scenario will contain the same development and commercialization decisions, Scenario 1 will act as the baseline for each of the other two scenarios your team will construct. It is important to begin with this page first, following your Planning & Alignment.

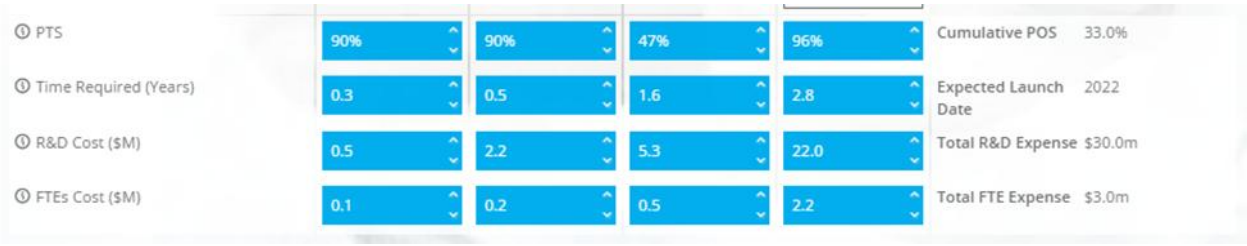
Your team will first make all development decisions starting in R0 and ending in Phase III. There are two steps to filling out these decisions most accurately:

1. Complete those decisions in previous development phases first, to reflect the known parameters of the development process to this current point

2. Then complete decisions for the current phase and future phases, to reflect the most likely development plan that your team constructs



If you acquire the asset in middle or late stage development you will still make development decisions that reflect those decisions of the former company. Those decisions will not impact your estimation of R&D costs or time-to-launch, as they have already been completed.



Below your clinical development decisions, you will find a table of the PTS, Time Required, R&D Cost, and FTE Cost for each Phase of development, as well as their cumulative effects for the entire development project. If your team feels any of these numbers are significantly different from reality, or you wish to reflect known information, you may manually adjust each of these values.

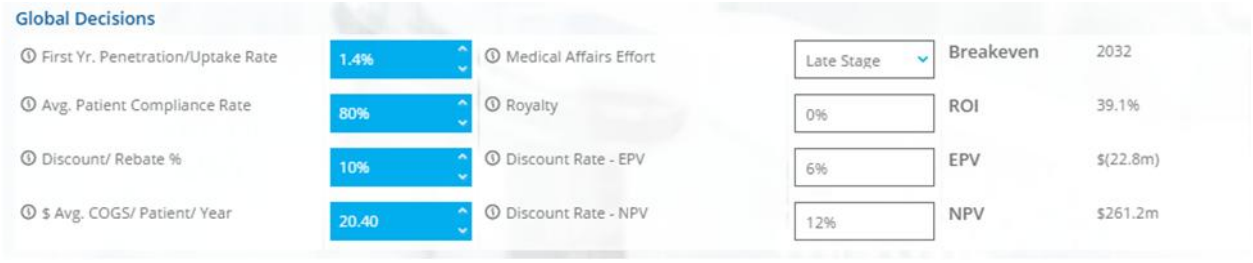
If you acquire the asset in middle or late stage development you will notice that time required and cost incurred for those phases are not included in the tables, to account for trials completed externally.

How do I account for regional differences as I launch this drug product?

Once you complete the clinical trial decisions, you will choose which regions you wish to enter, how much patient volume you expect in each region, and how you wish to support the launch with pricing and marketing investment. Each of these decisions will have a baseline value, estimated by the Tool. However, the price and volume decisions here are primarily independent of clinical development decisions, so your commercial team members should provide guidance as necessary to reach a realistic estimate.

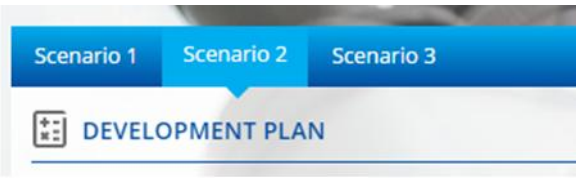
What commercial planning decisions do I need to make on a global scale?

Regardless of which geographic regions you enter, some decision will impact the value of the asset across all regions. Those decisions your team will make last, and are located at the very bottom of the Scenario Page. Each of these decisions will also contain baseline values, but you should manually update them based upon reasonable guidance from your commercial or manufacturing team colleagues.



How do I construct Scenario 2 and Scenario 3?

Once your team is confident that Scenario 1 is both an accurate picture of development decisions already made and a reasonable picture of the development plan through product launch, you may use Scenario 1 as the *baseline* for Scenario 2 and 3. You may move to either of the other two Scenarios by selecting that tab at the top of the Scenario Page.



To copy the baseline decisions and values onto the other two pages, select the Copy Base button on either of the other two Scenarios themselves.

When changing decisions on Scenario 2 or Scenario 3, remember to use your Dashboard metrics as your guide. If your team is attempting to create a *Best Case* Scenario, test which decision under your team's control will maximize those Dashboard metrics. If your team is attempting to create a *Worst Case* Scenario, test which decisions most decrease those Dashboard metrics. **Consider carefully the assumptions and risks from your Planning Page to guide your decision-making.**

How do I best compare the results across Scenarios 1, 2, and 3?

The Reports Page is the easiest way to compare results from one scenario to another. All data on this page is a result of the decisions made in the clinical development plan and in the commercial decision.

Guidance on interpreting this page:

A. Start with the Summary Table at the top, which displays each of the primary metrics Santen uses today to analyze its business success. Note where you see the biggest differences from one Scenario to the next. *Consider why you might see those differences.*

SUMMARY

Hide Scenario 2 & 3

	Scenario 1	Scenario 2	Scenario 3
ROI	184%	184%	184%
EPV	$4m	$4m	$4m
NPV	$637m	$637m	$637m
Peak Sales	$263m	$263m	$263m
Launch Date	2021	2021	2021
R&D Cost	$13m	$13m	$13m
POS	2.0%	2.0%	2.0%
Breakeven	2028	2028	2028
IRR	614.0%	614.0%	614.0%

B. With those differences in mind, look to the detailed reports below for explanations. Each of these detailed reports break up the critical metrics into their yearly values post launch.

Scenario 1

	Pre-Launch	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030
Net Sales	$0.0	$157.8m	$192.9m	$214.9m	$228.6m	$237.6m	$244.2m	$249.5m	$254.2m	$258.6m	$262.9m
COGS	$0.0	$7.3m	$8.8m	$9.7m	$10.1m	$10.4m	$10.5m	$10.5m	$10.6m	$10.6m	$10.6m
Gross Margin	$0.0	$150.4m	$184.1m	$205.3m	$218.5m	$227.3m	$233.7m	$238.9m	$243.6m	$248.0m	$252.3m
Research & Development	$13.8m	$1.6m	$1.9m	$2.1m	$2.3m	$2.4m	$2.4m	$2.5m	$2.5m	$2.6m	$2.6m
Sales & Marketing	$0.0	$11.9m	$14.5m	$16.2m	$17.3m	$18.0m	$18.5m	$18.9m	$19.3m	$19.6m	$20.0m
Royalty & Other	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Product Margin	-$13.8m	$82.2m	$100.6m	$112.1m	$119.4m	$124.2m	$127.7m	$130.5m	$133.0m	$135.5m	$137.8m
Operating Cash Flows	-$13.8m	$1.7m	$2.1m	$2.4m	$2.5m	$2.6m	$2.7m	$2.8m	$2.8m	$2.9m	$2.9m
Discount Cash Flows	-$13.8m	$1.6m	$1.9m	$2.0m	$2.0m	$2.0m	$1.9m	$1.8m	$1.8m	$1.7m	$1.6m

KeyMetrics

ROI	184.0%
EPV	$4m
NPV	$637m
Peak Sales	$263m
Launch Date	2021
R&D Cost	$13m
POS	2.0%
Breakeven	2028
IRR	614.0%

C. If you are focusing on a few specific decisions in the scenarios that impact those metrics of interest, adjust those decisions on the Scenarios pages. Then come back to this Reports Page to see their relative effects.

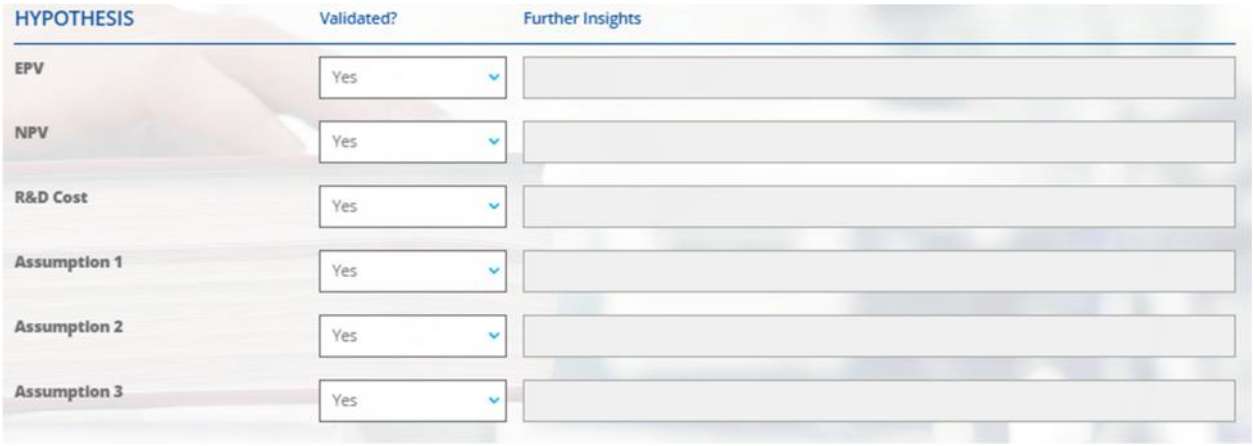
HOW DO I SUPPORT OUTCOMES? – COMMIT TO ACTION

Once you have finished constructing your three scenarios, the last page you will complete is the Commit to Action Page. Here, the purpose is to generate insights from your original hypotheses, and commit individuals to specific action following the Meeting.

How do I test whether the Tool supports my team's hypotheses for development?

On the top half of the Commit to Action Page, you will find 6 items listed directly from your Action & Planning responses: the 3 primary metrics and the 3 primary assumptions.

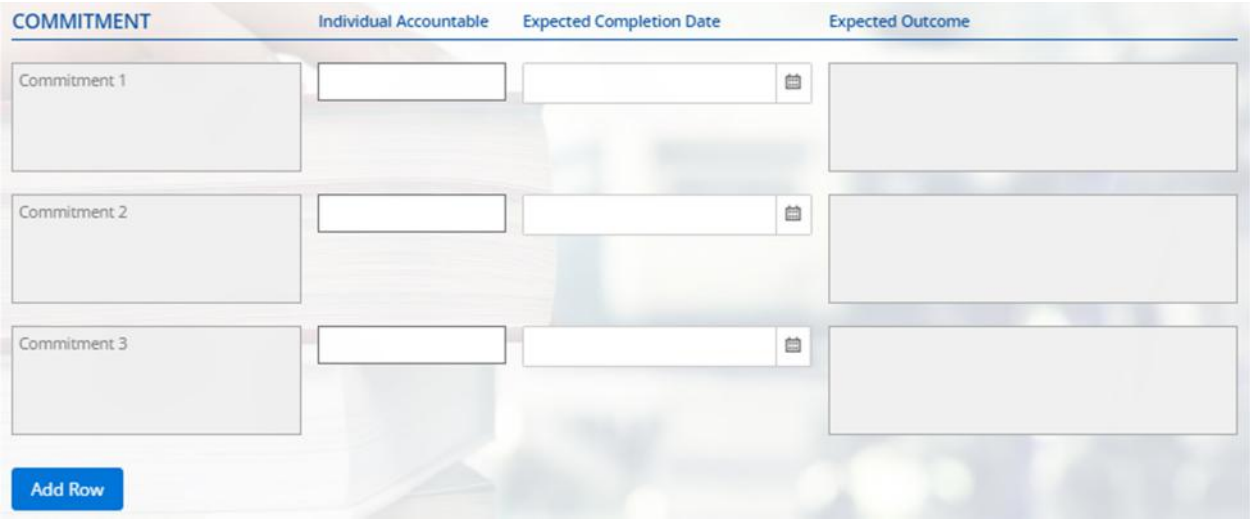
1. For each primary metric, mark whether it has been *validated* or not, meaning that your scenario analysis supports this as critical to this program's success or proves that another metric is more important.
2. For each assumption, repeat this process, indicating whether that assumption is correct based upon your analysis or requires adjustment.
3. For each item that has been validated *(indicated as a Yes)* explain why your scenario analysis supports that validation. What have you learned that leads to this outcome?
4. For each item that has not been validated *(indicated as a No)* explain why your analysis disproves that hypothesis. What have you learned that leads to this outcome?



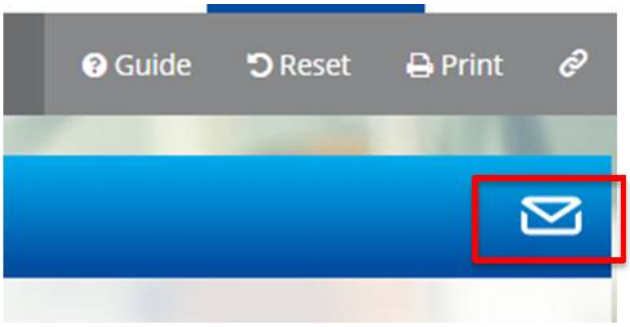
How do individuals on my team commit to actions?

As the final step in every Meeting, each individual on the team should think of *one action* they can take that would support the insights just created above. With greater clarity of the project critical metrics and what impacts them, what can the individual do to support that metric? With greater clarity on project assumptions, what can the individual do to support that assumption? Each action requires four criteria to be considered complete:

1. A clear description of the commitment
2. The name of the individual accountable for the action
3. The expected date by when the action will be complete
4. An estimation of what the action's impact will be on the business



When all individuals have entered an action into the Tool, select the Mail icon beside the actions chart. This icon will open an e-mail window and populate an e-mail with each of the individual commitments, names, dates, and outcomes. You may then send this e-mail directly to the team as a summary and confirmation of all commitments made by individuals.



It is your responsibility as the PM or GPL to follow-up with these individuals at their expected completion dates to assess the impacts that their actions have had.

WHAT IS A POSSIBLE SCENARIO WHEN I MIGHT USE THIS TOOL?

Below is a description of one possible scenario to us as an example for your team. It shows how the Tool leads to further insights and plans for drug product development. Please note, while this scenario is based off of a Santen asset, the exact market data, profile, and development strategy have been altered from the original plan.

What do we know about this asset's target product profile?

DE-999 is intended for the treatment of Glaucoma by acting as a FP/EP3 Dual Agonist. It increases the aqueous humor outflow via both conventional and uveoscleral outflow. Current dosing requires manually applying eye drops three times a day. The primary patient population under investigation is those with treatment naïve ocular hypertension. While there is potential to treat patients who are non-respondent to the current standard of care, efficacy of current trials does not yet indicate high probability of successful intervention.

What were the terms of the acquisition?

We have acquired DE-999 following R2 for a $10 million USD cash upfront milestone payment, and 5% royalties if fully commercialized. All CMC responsibility has been turned over to you moving forward, and the estimated costs of manufacturing per patient/year is $30 USD.

The current API patent expires in 2030. There are concerns within our organization that we may not reach breakeven until after LOE, increasing pressure to deliver with expediency.

Where are we currently in terms of development?

We have acquired this compound following pre-clinical research, and are now considering first-in-human Phase I trials. The licensing company has only run preclinical trials though R2, all of which occurred in Japan. Toxicology and ADME results were promising, showing insignificant dose-dependent adverse effects across relatively high and low dosage strengths alike. However, the licensing company did not invest in additional biomarker research, and therefore further insight into exact patient profiles is not available beyond the above.

Current estimates indicate a target launch date of 2023. However this estimate assumes a local product launch in Japan and Asia, and does not account for timeline delays if we choose to launch in other global regions. It also assumes slightly shorter than average trial observation periods, and moderate sized patient populations that will not require significant time to recruit. Both assumptions are made given the regulatory nature of Japan and Asia.

What do we know about the market conditions of this drug?

While Glaucoma was once the largest ophthalmology market, it has since shrunk due to the patent expiration of the standard of care in 2010. However, it has recovered recently, with two patented drugs on the market in the U.S. and Europe. 90% of patients on treatment are using one of these two drug products due to their superior efficacy. Market entry outside of Asia and Japan is therefore difficult given superiority of such standard of care. Further, regulatory pathways in both the U.S. and the EU have been increasingly more rigorous in recent years.

Given DE-999's primary indication, the Japanese market is approximately 1.3 million patients and the Asian market approximately 500 million patients. Given current competitive market conditions, your marketing team is conservatively estimating 10% market share in each region as a base case, with an average yearly price of $300 USD in Asia and $250 USD in Japan.

What questions face our development team?

- In this early development stage, what clinical-trial formulation would maximize EPV?
- Given difficult regulatory pathways in the U.S. and EU, how can we maximize POS across multiple regions?
- Given looming LOE, how can we minimize time to D3 and preserve a high POS?
- Given such late-stage uncertainty, what backup plans can we construct to support POS?

PRE-MEETING BRIEFING

*The purpose of this **Pre-Meeting Briefing** is to inform you of the Tool that you will be using during your Planning Meeting, and provide brief preparatory work to complete in advance.*

TOOL PURPOSE:

The Tool you will use during your upcoming Meeting will allow program planning teams to make more efficient and informed decisions during planning and forecasting meetings. To accomplish this, you and your team will:

1. *Learn to identify which development decisions most impact your asset's value*
2. *Understand how decisions create value or create further risk*
3. *Evaluate and communicate your asset value to & from other functions*

HOW YOU WILL USE THE TOOL:

The Tool is designed to be used during your development planning meeting, both during early stage development (R2 / D1) and late stage development (D2 / D3). The Tool is not intended for individual use, and is not to replace forecasting tools currently used by the Project or Portfolio teams. The Tool will guide your team through three parts of the meeting: (1) first creating alignment about the Tool's use; (2) then generating insights about development decisions and scenarios are most important for success; (3) and lastly supporting action from each team member, including yourself.

As your team uses the Tool, you will create different development scenarios. In each scenario, you will change different development decisions and see how they impact your development metrics directly. This will allow you to decide which actions are most import to improve your development's success. It will be the role of your Project Manager and/or Program Leader to lead the team through the use of the tool, and they have been trained on its use. However, proper decision-making within the tool will rely on *your* functional expertise and that of your functional colleagues.

YOUR RESPONSIBILITIES:

To prepare for the meeting, please complete the following page **in the next week** and return a completed version to your Meeting Leader. Please answer each of the question in regards to this current asset under development, and consider your function's role in that development. Each of your other team members are completing an identical document. It will be critical to build alignment at the beginning of the meeting from each of your answers.

Your Meeting Leader decided that the most important metrics for this asset are:

EPV		

How do you support these three metrics during asset development?

Example: I improve EPV by increasing initial patient uptake of the drug product post-launch.

What information do you already know about this asset? What more information do you want to know to support these metrics?

Example: I know that the product is easy/difficult to administer. How easy is it to manufacture?

What are three (3) assumptions or risks during asset development that would strongly affect its success?

Example: One assumption is that the asset is more efficacious than the standard of care.

What asset development decisions will have the biggest effects on the three metrics above?

Example: We can increase EPV and patient uptake with earlier involvement of Medical Affairs.

In this development's timeline, what are the next decisions that are your responsibility?

Example: In my function, I am responsible for *this* during the next stage of drug development.

TOOL FINANCIAL GLOSSARY

Breakeven – The year in which the amount of total investment in a product or asset is equal to the operating margin or return of that asset from sales.

COGS (cost of goods sold) - The total accumulated manufacturing cost of producing a finished drug product, including direct labor, raw materials, and overhead.

Discounted Cash Flow – Discounted cash flow estimates the future value of operating cash flows by reducing that cash flow by the appropriate yearly discount rate; discounted cash flow helps determine the future potential for current investments.

Discount Rate – Percentage used to decrease the present value of future cash flow. A discount rate takes into account the diminishing value of cash over a period of time, as well as the greater uncertainty of future cash.

EPV – Adjusted net present value by multiplying the values of current cash outflows and future cash inflows by the probability of success; EPV accounts for uncertainty and risk that is not accounted for in NPV**.**

FTE Expense – Overhead expense of company-employed full time equivalents, or employees, during the development of a product.

Gross Margin - Indicates how efficient a company is at managing cost of goods sold and translating revenue into operating cash flow; Defined as gross profit divided by net sales.

IRR (internal rate of return) – The discount rate that makes the net present value of all cash flows from a particular asset or product equal to zero; a higher internal rate of return signals a relatively more valuable project.

Net Sales – Net sales are generated from the sale of products to consumers; Can be calculated as price per product multiplied by volume of product sold; Revenue is often referred to as net sales.

NPV (net present value) – The difference between the present value of cash inflow from operations and the present value of cash outflows from operations; this present value is determined after accounting for the discount rate over the number of years of product sales.

Operating Cash Flows – The amount of cash generated by a company's normal business operations; Positive operating cash flow indicates that a company can maintain and grow its operations.

Operating Margin - A measurement of what proportion of a company's revenue is left over after paying for the variable costs of production, such as wages and raw materials. It is the ratio of operating profit divided by revenue, usually presented as a percentage and sometimes as an amount.

Peak Sales – The greatest amount of net sales generated in any one particular year of the sale of a product.

POS (probability of success) – The probability of observing success in the future given the currently observed data and the value of the treatment effect.

R&D Cost – R&D cost is the sum of all expenses associated with both the research and development of the company's goods or assets.

Rebate – Proportion of net sales that are reimbursed to the customer of the product; a rebate reduces the actual price of the drug product to the customer.

ROI (return on investment) - measures the gain or loss generated on an investment relative to the amount of money invested. ROI is usually expressed as a percentage and is typically used to compare a company's profitability or to compare the efficiency of different investments.

Royalty - A payment made by one company to another that owns a particular asset for the right to ongoing use and development of that asset; Royalties are typically agreed upon as a percentage of gross or net sales derived from the use of an asset or a fixed price per unit sold.

Sales & Marketing Cost - The sum of all direct and indirect selling expenses and all general and administrative expenses, including HR, Finance, Legal, and other support organizations.