IQVIA BIOTECH

White Paper

CAPTURING THE ATTENTION OF INVESTORS

The creation of a compelling value story

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INTRODUCTION

Finding a promising lead drug candidate is an important moment to celebrate; it's the initial step on the route to market and to improving patient outcomes. However, it is just the beginning. The next step – drug development – is your opportunity to learn about your drug's clinical profile in patients. It will also showcase to investors that your drug candidate has the potential to meet patients' unmet needs and see success in the market.

Embarking on a drug development program is lengthy and costly, and emerging biopharma companies need to get their candidate on a development path offering the highest opportunity for success: to generate the right data at the right time, attracting investors and continuing that momentum through clinical development.

The first task is creating a product value and vision, the process of which can be broken down into three essential elements:

TARGET PRODUCT PROFILE (TPP)
Captures the product vision and development goals for the product in an indication. Forms the foundation for the clinical development plan and understanding commercial value.

CLINICAL DEVELOPMENT PLAN (CDP)
Involves iterative planning through scenario generation. Enables important decision-making based on time, cost and risk trade-offs, which impact investment.

EXPECTED NET PRESENT VALUE (ENPV)
Places an objective potential value on the product at the end of the projected development path or paths. Is based on the development time, cost, risk and return assumptions for each possible scenario.

The TPP, CDP and eNPV are not only important to investors, but for alignment of your own development team. It is also the base for creating the clear product vision that underpins the value of the drug to the patient, the physician and the payer. Creating a realistic and robust value story will improve the chance of successfully funding your development program and gaining approval of your drug.

WHERE ARE YOU GOING?

ARTICULATE YOUR PRODUCT VISION

The development of a drug begins with choosing the indication and patient population, creating a TPP and understanding the competitive landscape.

For many drug candidates, there are a number of potential indications that are revealed during pre-clinical development. In order to plan the development path, these need to be prioritized by asking the following questions:

- Which will be the first indication to push through clinical trials?
- Are there indications that can be developed in parallel?
- Which indication can be used to extend the product life cycle?

Making the initial choice: Finding the best indication to start your journey

Understanding the issues that are most important to the company helps at the beginning of the indication selection process. These include:

- Development timelines to key data
- Likelihood of successful clinical outcomes
- Link to the mechanism of action and a variety of other potential variables
- Size of market need
- Organizational goals

Having the right data in hand to help see the differences in these parameters is extremely important for confident decision-making. The types of data that can help to shed light on an indication prioritization are shown in Table 1. In general, companies have three main constraints to balance in determining the optimal path forward during drug development:

TIME

How long will development take to a critical value inflection point? Time-to-market or to proof-of-concept (PoC), or another point?

COST

How much money will it take to get there?

RISK

What is the chance of the drug making it successfully through development?

Development in different indications will have different impacts on time, cost, risk and ultimately return on investment for a drug. These impacts should be evaluated so that the company can strike the right balance and make a properly informed decision on the right path forward. In order to do this, scenarios can be generated to compare aspects of these constraints. This way, companies can see the trade-offs in time, cost, risk and return, and make a well-informed decision that is justifiable to investors or other key stakeholders.

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Table 2 shows an example of an evaluation of development trade-offs in a situation where a company is trying to decide between three possible indications for their drug. In this example, the focus is on the fastest route to PoC while keeping risk reasonably low and maintaining a high value. As with many small companies, the key constraint for this company is limited funding through the point of initial PoC data. In this example, psoriasis was the best choice as it offered the best balance between low clinical and regulatory risk, fast and relatively inexpensive PoC potential and high overall value.

The more real world data can be used to justify decision-making throughout the drug development process, the more confidence the development teams, board members and investors will have in the selected path forward.

Two stages to creating the TPP

The TPP is an essential tool that defines the product concept, links the commercial and development strategies, and forms a vital part in the development of the value story. The more data that is in the TPP, the more useful it will be.

Stage 1

As a single, evolving document, the TPP should contain the commercial goals and clinical requirements for the product in the indication, aligned to the science and regulatory requirements in that space, and also include payer needs for reimbursement.

Table 1: Using data to support decision-making

	RECRUITMENT DATA	STUDY COST DATA	EPIDEMIOLOGY DATA	PRESCRIPTION DRUG DATA	MEDICAL CLAIMS OR HEALTH RECORD DATA	MARKET DATA
TIME TO PoC	✓					
COST	✓	✓				
RISK						
TIME TO APPROVAL	✓					
RETURN ON INVESTMENT	✓	✓	✓			✓
UNMET NEED			✓		✓	✓
REGULATORY PATH			✓			
COMPETITION				✓	✓	
OPERATIONAL CONSIDERATIONS			✓		✓	

Table 2: Data-backed insights allow for evaluation of trade-offs

		TIME		COST	RISK		VALUE
	INDICATION	TIME TO PoC	APPROVAL DATE	DEVELOPMENT COSTS (TO PoC)	PIVOTAL ENDPOINT	REGULATORY PATH	VALUE (PEAK SALES)
	RHEUMATOID ARTHRITIS	2 years	2029	$220M ($45M)	ACR responder	U.S.-Guidance	$600M
✓	PSORIASIS	1.3 years	2027	$180M ($28M)	sPGA/PASI	U.S.-Precedence	$800M
	JUVENILE CROHN'S DISEASE	2.5 years	2025	$65M ($28M)	Crohn's disease activity index	U.S.-Precedence	$300M

Importance: Time to PoC, low risk, product value
Constraints: Limited funding

Note: Values are for example purposes and do not represent actual data

Stage 2

As the drug moves through development and the evidence base grows, the TPP should be revisited. Commercial assumptions made based on the profile should be updated accordingly.

TPP development should ideally begin prior to Phase I since this is a foundational document for the development strategy, but if not, it is essential prior to Phase II or the company risks misalignment between clinical data and commercial needs. Companies may also develop additional TPPs for different indications.

Understanding the competition

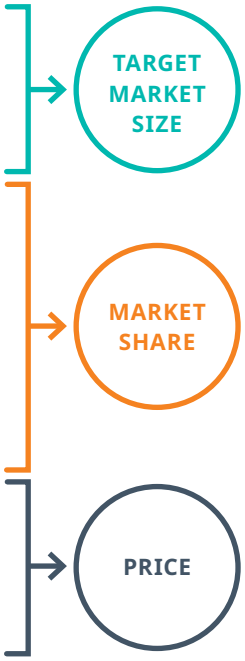
Part of the understanding of market size and share must be based around knowledge of the competition, including both the current competitive landscape and where it could move in the future, when the candidate drug is likely to reach the market. It will help the company to understand where the drug will fit within the market landscape and how it will stack up, not only against current competitors, but also those that may hit the market around the time of its launch.

The assessment of the competitive landscape should:

- Begin as early as possible in drug development
- Use the information gained to support development decisions, including the choice of indication, unmet need within a subpopulation and areas for clinical differentiation

Table 3: Sample TPP as the basis for commercial value

PRODUCT GOAL	BASE CASE PROFILE
Indication	Indicated for the treatment of patients with moderate-to-severe plaque psoriasis who are candidate for phototherapy or systemic therapy
Patient Population	Adults with moderate-to-severe plaque psoriasis who are candidates for phototherapy or systemic therapy
Dosage Form/Regimen	100 mg tablet taken once daily
Clinical Efficacy	• 40% PASI-75 responders vs 5% PBO • 25% Static Physicians Global Assessment (sPGA) responders vs 5% PBO • Time to onset within 2 weeks (50% PASI-50 responders) • No tolerance/rebound following withdrawal
Safety	• GI disturbance less than 5% • No drug-drug interactions
Quality of Life (QoL)/ Payer Needs	• Improvement in QoL over Minimal Clinically Importance Difference (MCID) vs PBO • Improvement in symptoms over MCID vs PBO • Comparator data
Other Important Aspects	• Development partner to support non-derm indications following PoC • U.S. and EU development in parallel



- Shape clinical trials to generate data that supports important points of differentiation between the target drug and its competition, from the perspective of the patient, physician and payer.

HOW DO YOU GET THERE?

CHOOSE THE RIGHT DEVELOPMENT PATH

The development path for a new drug isn't always clear or linear. There are many points where decisions have to be made which almost always impact time, cost and risk (and ultimately return).

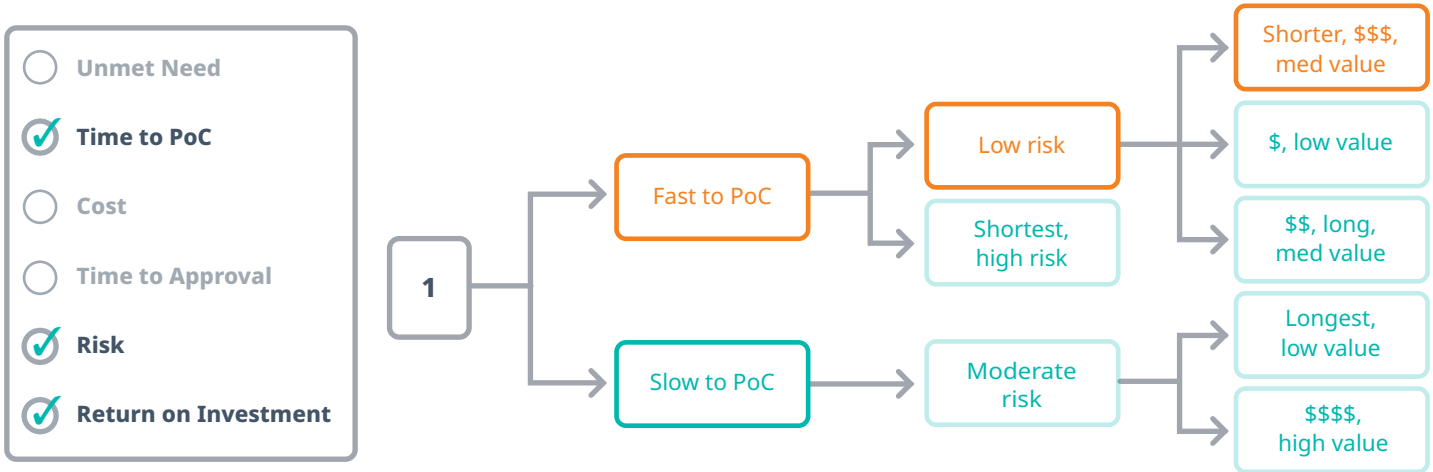
To find the right development path, companies need an understanding of the design elements and alternatives and an ability to assess the impacts of these on time, cost, risk and return. To do this, companies will recognize their viable alternatives and map out the different options, including key decision and investment points, both at a program and study level.

As an example, options that reduce study-level or program-level risk may increase the time and cost required but improve the chance of getting to market without having to repeat a study or Phase III program, therefore improving the chances of seeing a positive return on investment.

The more real world data can be used to justify decision-making throughout the drug development process, the more confidence the development teams, board members and investors will have in the selected path forward.

Once it's clear which of the variables are most important to the company – and these may not be the same for all projects – it will be clearer how to prioritize amongst different development options. Figure 1 shows an example of the path taken by a company for a well-funded project where the shortest time to PoC, lower risk and higher return are the most important variables.

Figure 1: Choosing the right path



WHAT IS THE VALUE OF YOUR APPROACH?

CONVINCE STAKEHOLDERS TO JOIN YOU

One of the ways to measure value with a degree of objectivity is to combine the three value inputs – time, cost and risk – with return on investment to create a single metric. This is known as the expected eNPV (see Figure 2).

This approach brings all the pieces together to provide a snapshot of the candidate drug in a specific market and indication at the present time. The eNPV provides stakeholders with a robust and neutral viewpoint, and can be used to compare different pathways, molecules or indications, while also demonstrating the impact of trade-offs.

This ability to provide a convincing value at any given point, and for any given pathway, is particularly important for emerging biopharma companies seeking investment. These smaller companies are under greater pressure to demonstrate value and for them, costs are a major influencing factor in decision-making.

Despite its usefulness, both for internal monitoring of projects and for external communication, eNPV is still better understood in financial circles than by drug developers. In an IQVIA™ Biotech poll, fewer than a third of those asked were very familiar with the approach (see Figure 3).

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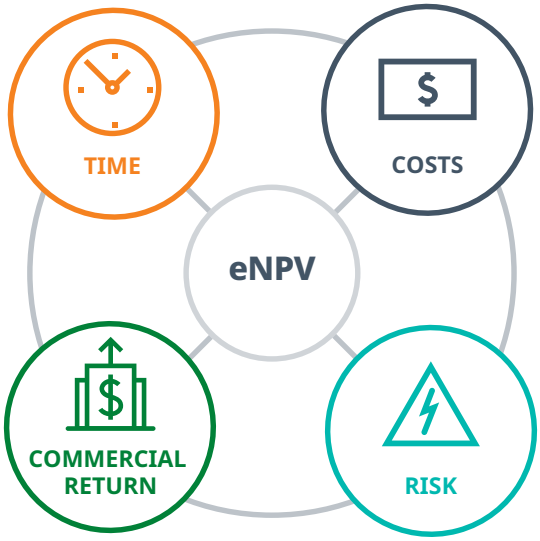
Figure 2: eNPV as a unifying metric



eNPV = Expected net present value

- Development durations
- Development and commercial costs
- Probability of technical success
- Potential market share and revenue

Figure 3: Poll question – How familiar are you with using eNPV in clinical plan optimization?

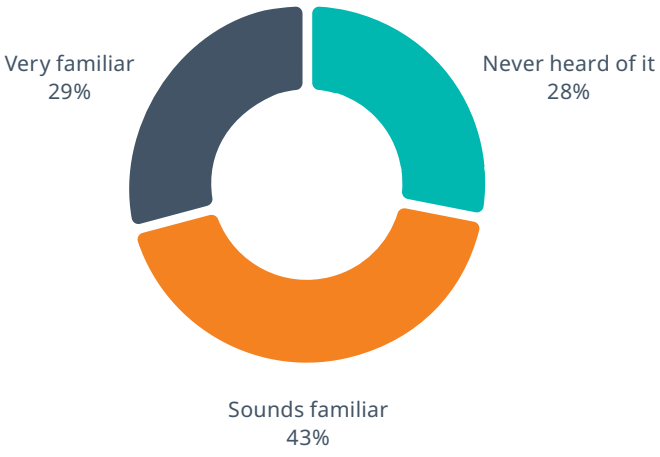
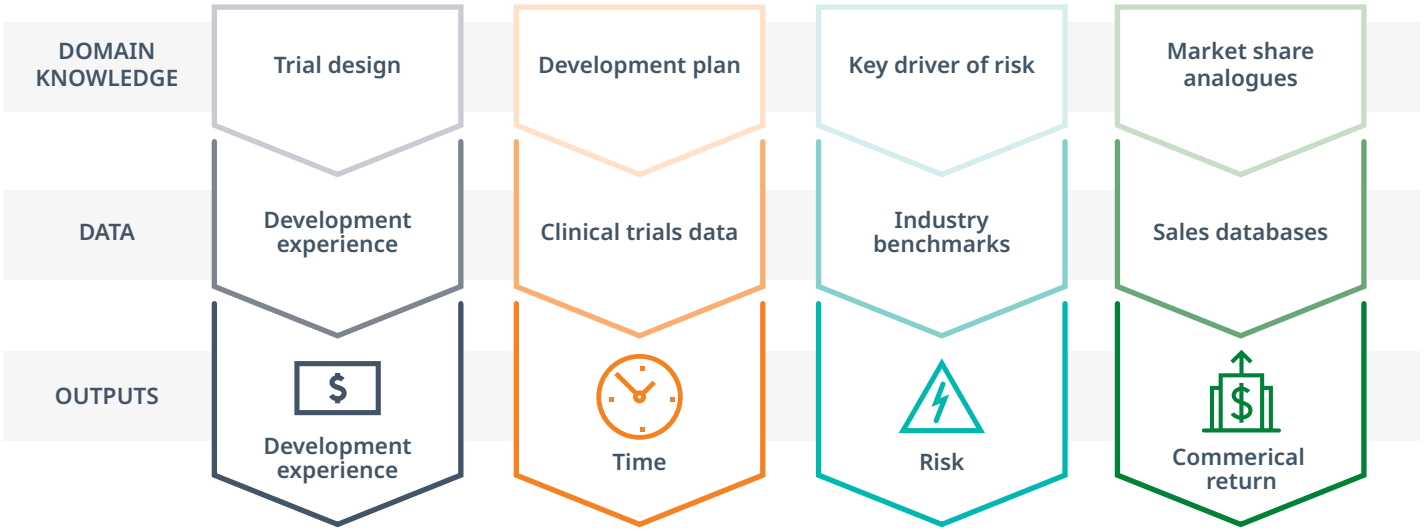


Figure 4: Data-informed planning for robust decision-making



Putting eNPV to work

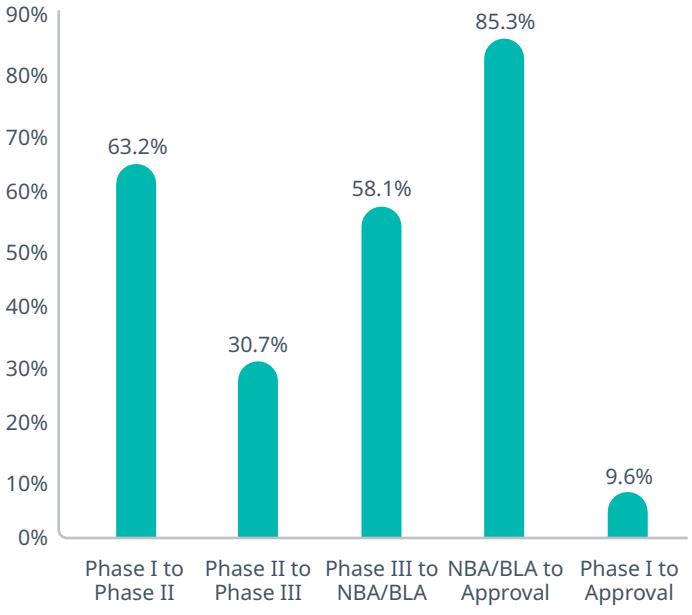
The key function of eNPV is to enable developers to compare alternative approaches based on variations of time, cost, risk and return. To get the most robust outputs from the eNPV approach, it's important to use the best inputs in data and domain knowledge. As shown in Figure 4, the appropriate domain knowledge and data varies according to the required input.

As an example, when looking at costs as an input, there are databases that contain sample trial costs, but these may need to be altered according to domain knowledge about the size and complexity of studies.

Similarly, with time as an input, data is available on lengths of trials, but this information needs to be balanced against past experience and trial design. For both time and costs, it's important to be realistic, not optimistic. Return on development can be based on data from sales databases, but will also depend on disease epidemiology and competition at the time of launch.

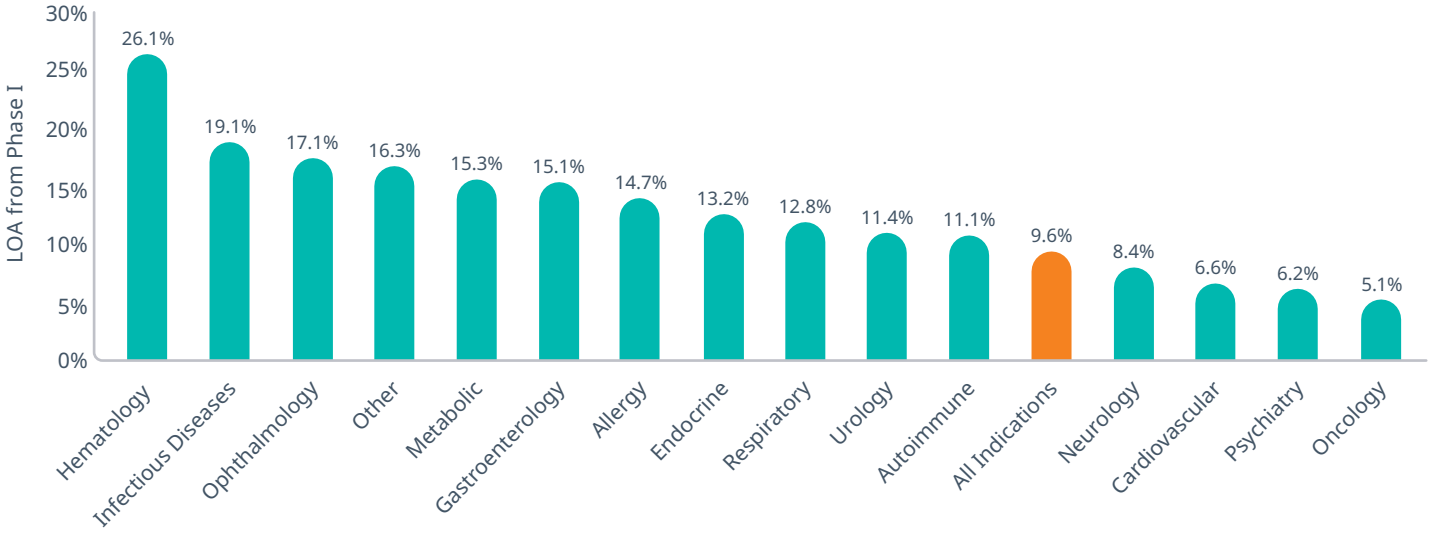
Risk prediction needs to consider the probability of drug candidates advancing into the next phase (see Figure 5).

Figure 5: Probability of success in drug development for all diseases and modalities – Overall



Source: Clinical Development Success Rates 2006-2015 – BIO, Biomedtracker, Amplion 2016

Figure 6: Probability of success in drug development – By therapeutic area



Source: Clinical Development Success Rates 2006-2015 – BIO, Biomedtracker, Amplion 2016

For most programs, the chance of moving from Phase I to Phase II is relatively high, but the step from Phase II to Phase III is much harder, as this is the stage where drug efficacy (as opposed to drug safety) must begin to be shown. Even after all the data from pivotal studies is in place, there is still on average a 15 percent probability of failure of acceptance of a drug submission for approval. Overall, the probability of success from Phase I to approval is less than 10 percent.

Domain knowledge of therapeutic areas is important when choosing indications and calculating eNPVs, as different indications have different historical chance of approval. As shown in Figure 6, hematology, infectious disease and ophthalmology have the highest approval rates, while cardiovascular, psychiatry and oncology have the lowest rates.

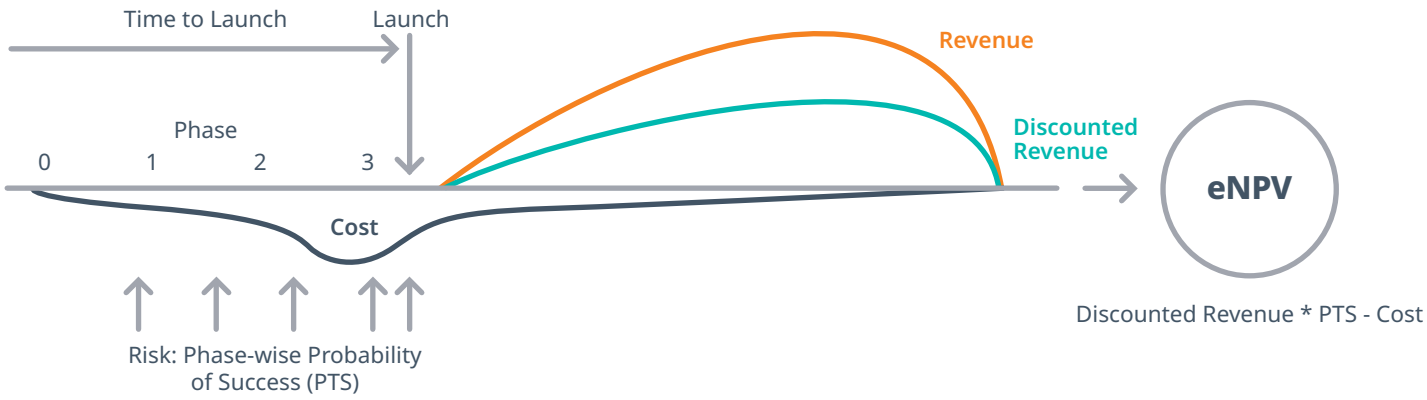
In contrast, with rare diseases, the chance of approval is much higher, averaging 25 percent between Phase I and approval. Competition is often less, and the final price achieved for drugs is likely to be high.

However, clinical trials in rare diseases can be harder to recruit as the pool of trial candidates is smaller, as is the market once the drug is launched. Phase I-to-approval probability is slightly lower for chronic, high-prevalence indications, averaging nine percent. In this market, price following approval is likely to be low unless the value story is strong, and competition will be high, but the market size will be much larger.

Drug type plays a part in estimating risk too. Biologics and reformulated small molecule drugs have higher approval rates than innovative small molecule drugs. This is because biologics tend to have better safety profiles, particularly in oncology, and reformulated drugs have a lot more safety and efficacy data behind them, reducing the risk of failure at each step.

The challenge is to bring all these factors together to create an eNPV that can also consider the impact that future discounting will have on return on investment (see Figure 7).

Figure 7: Assessing risk from pre-clinical through to launch



Optimizing eNPV through scenario modeling

The strength of the eNPV process is the ability to model the impact of different pathways and approaches and compare them using a standardized metric. In the following example, three different approaches – "Conservative," "Standard" and "Aggressive" – differ in terms of number of patients, studies and time to launch, but they can all be compared in terms of the resulting value of the drug development approach (see Figure 8 on the following page).

The strength of the eNPV process is the ability to model the impact of different pathways and approaches and compare them using a standardized metric.

Aggressive:

- This is the highest risk approach, with the greatest chances of drug failure before PoC or market
- The development time is the shortest
- The eNPV is the lowest, but the time to return on investment is sooner than the other approaches, which could be used to attract investors

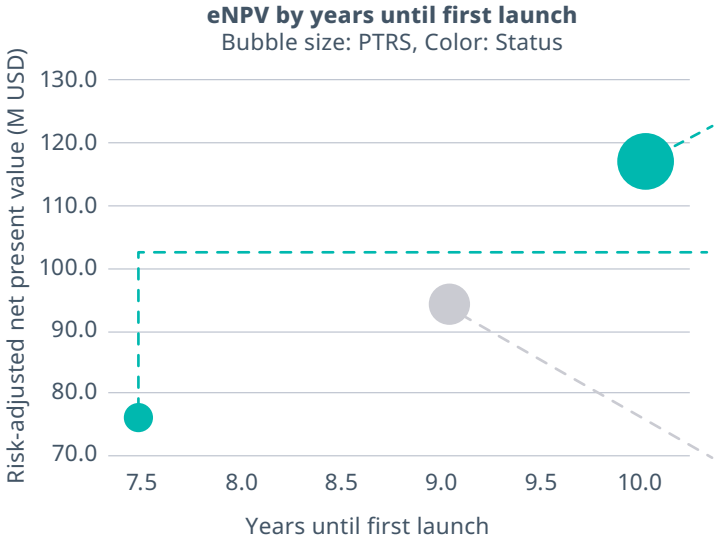
Conservative:

- This approach uses larger studies and stringent criteria for the go/no-go decision between Phase I and Phase II (also described as the "fail fast" approach)
- It has a higher chance of getting the drug through Phase III and submission for approval by increasing the number of doses studied in earlier phases
- The overall program is longer, and therefore the costs are higher and the launch date is further out
- However, it has the highest eNPV, which could be used to encourage investors to sign up to a longer end game

Standard:

- The standard approach sits between these two

Figure 8: Scenario planning for time, cost and risk trade-offs



STATUS: WHAT-IF			COST
Conservative	Launch: **May 2028** Yrs. until first launch: **10.1**	PTRS: **30.0%** eNPV: **116.9**	**$264.3M**
Aggressive	Launch: **Sep 2025** Yrs. until first launch: **7.4**	PTRS: **12.6%** eNPV: **75.2**	**$179.0M**
STATUS: BASELINE			
Standard	Launch: **May 2027** Yrs. until first launch: **9.1**	PTRS: **20.5%** eNPV: **94.3**	**$220.8M**

CAPTURING THE ATTENTION OF INVESTORS

THE CREATION OF A COMPELLING VALUE STORY

The development and optimization of the drug development path is an important part of creating a compelling value story; both the TPP and eNPV are vital tools in this process. The eNPV metric allows organizations to align business drivers with the product goal. The next step is the choice of the development path, which relies on trade-offs. Once these factors have been determined, the final step is persuading the stakeholders to agree on the right path by using informed and data-driven decisions.

The key takeaways

ARTICULATE THE PRODUCT VISION

- Translate scientific information to meet the clinical approach

Prioritize indication based on data, unmet need and market opportunities	Create a TPP	Understand the competitive profile

UNDERSTAND THE DEVELOPMENT PATHWAY, INCLUDING TIME, COST, RISK AND DECISION POINTS

- Plan clinical development to deliver the TPP

Ensure that data considers robust time and cost estimates	Ensure robustness in understanding alternatives/trade-offs	Be prepared to defend plans

- Use the development pathway to enrich the pre-investigation new drug approach

Meet with authorities to understand risk from a regulatory perspective

CONVINCE STAKEHOLDERS OF ASSET VALUE

- Have an early and accurate forecast model

Provide enough information to inform stakeholders of the possibilities

- Understand time, cost, risk and revenue impact

Create a valuation in terms of risk-adjusted eNPV

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