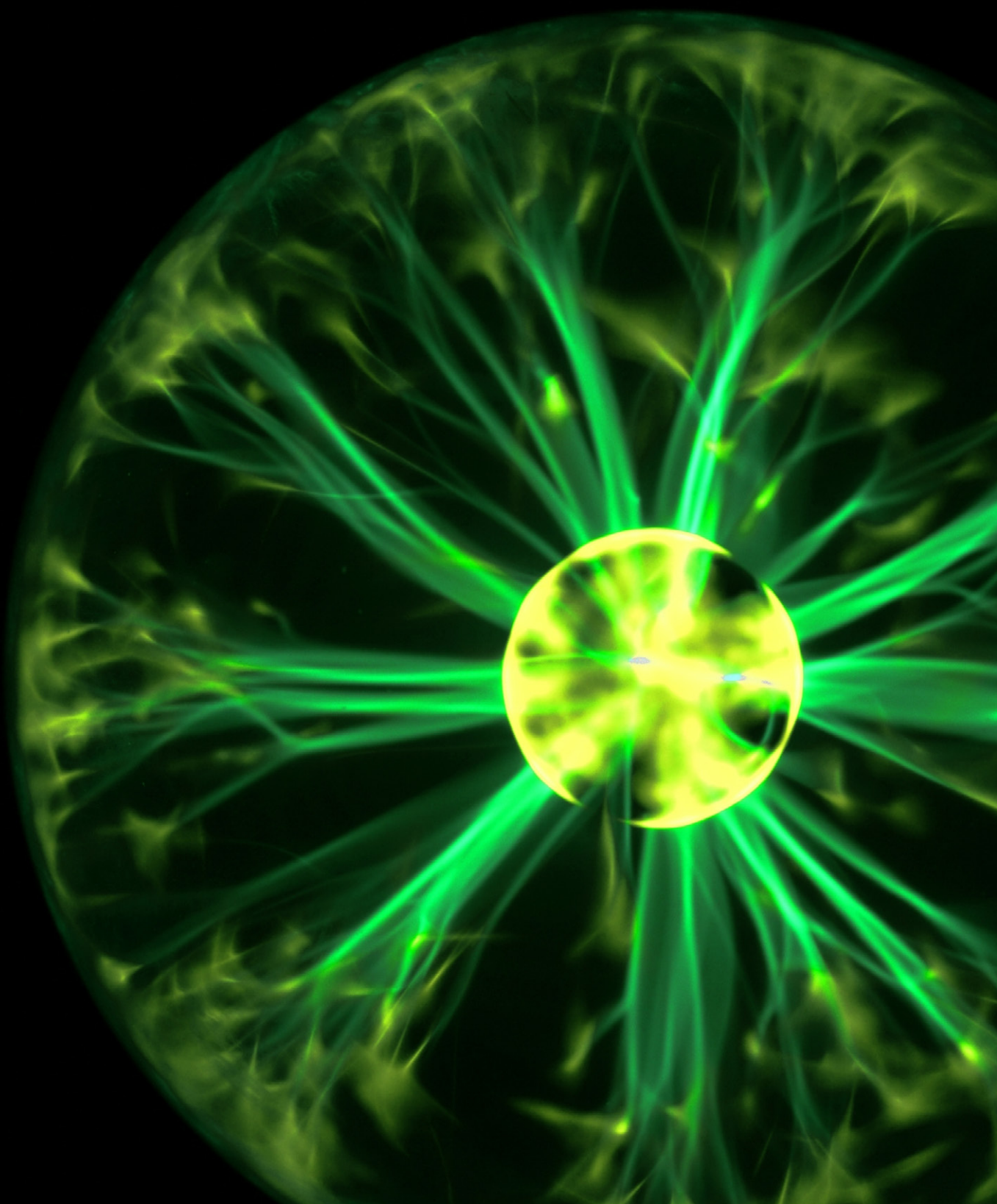


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Early Value Assessment

Optimizing the upside value potential of your asset

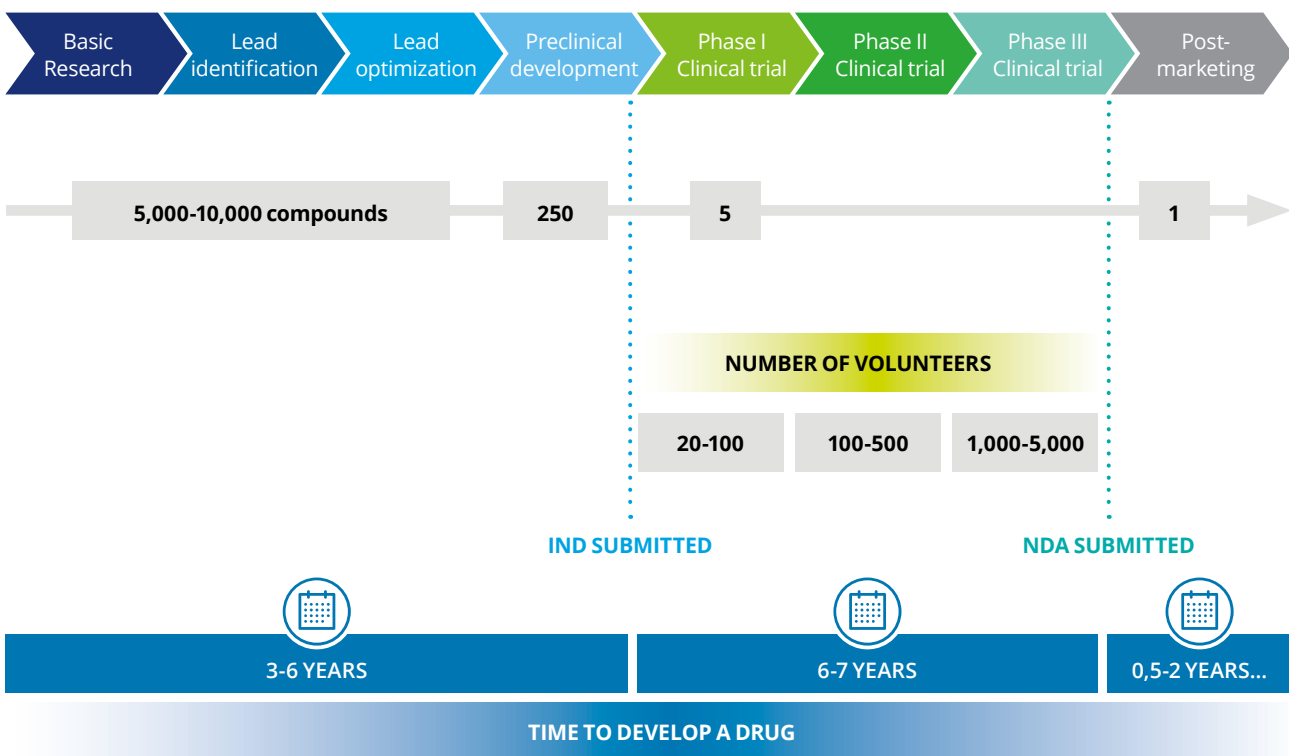


Promising science does not always translates into a blockbuster

New lead drug candidates coming out of the discovery phase typically look very promising with a high potential to improve patients' outcomes and with high commercial expectations. However, this is only the first step in the long journey to reach the patient.

Translating a promising discovery into a new therapy is a costly, lengthy and risky process, with an average cost of \$2.6 billion (value in 2013 USD) and an average development time of 12 years. Only 5 in 5,000 drugs that enter preclinical testing will progress to human testing, and only one out of these five drugs will get approval. Those are not very good odds.

Figure 1: Time to develop a new medicine to the standards of quality, efficacy and safety laid down by legislation.



- From initial discovery to the marketplace takes **about 10 to 15 years** for a new medicine.
- Each **5,000 to 10,000 compounds** that enter to the pipeline, only 1 receives approval.
- Medicines that reach clinical trials have only a **16% chance of being approved**.
- The **average R&D investment** for each new medicine is around **\$1.2-1.5 billion**, including the cost of failures.

Taking an early-stage asset from bench to bedside - how to attract investments

It really requires specialist expertise to move a candidate through development, clinical testing, formulation, regulatory submission, marketing approval, manufacturing certification, and market launch. Indeed, advancing a candidate from “bench to bedside” requires massive financial resources, as well as deep technical and commercial knowledge.

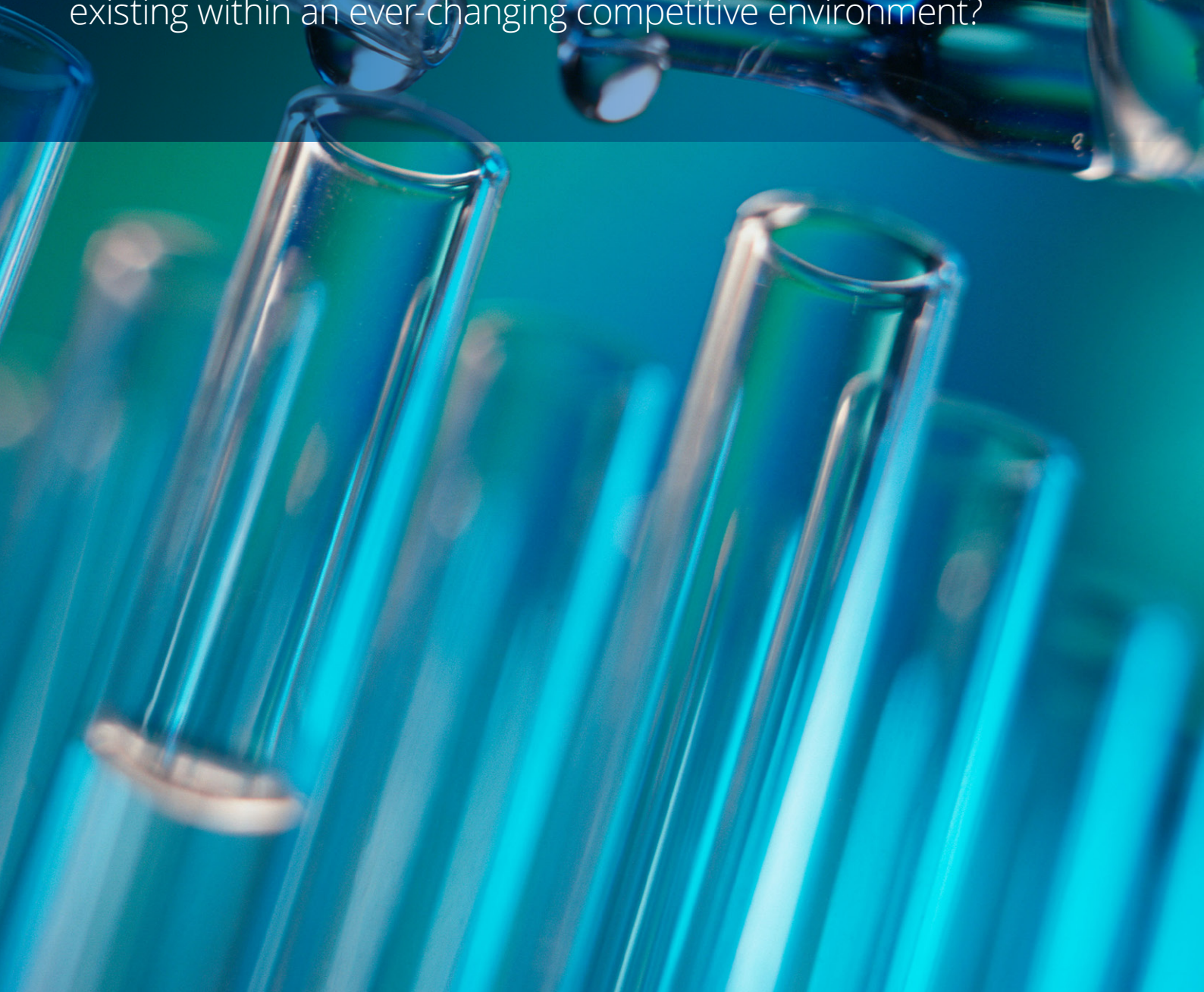
Biotech start-ups have to rely on investors (e.g. venture capital funds, business angels or institutional investors), Partnerships or Mergers & Acquisitions to access this financial support and technical and commercial expertise. Early-stage innovators will need to develop an accurate assessment of the probability of scientific, regulatory, and commercial success of the asset, in order to advance the interests of investors, which will allow these collaborative investor relationships to develop successfully. A comprehensive, data-driven and objective understanding of the value of the asset is key to acquiring funding for a promising science initiative.

Early value assessment is a powerful tool to demonstrate to investors the upside value potential of the asset. Armed with this information, early-stage innovators can better understand their own value story and be prepared to enter partnership discussions from a strong negotiation position, and to use this information to help maximize funding.



Predicting the future

A key question then becomes - how can an early-stage innovator put a reliable price tag on an asset that offers a promise of success within a 12-year time horizon, and which involves high risk and high development costs, all while existing within an ever-changing competitive environment?



Understanding value

As the saying goes, "if you do not know where you are going, it does not matter how you get there." Having a clear and well developed business objective provides direction, and the criteria for the decision-making process. This will ensure consistency and coherence in all actions and decisions, which will need to be made along the way.

The concept of value might be intuitively understood - the idea that an early-stage asset will provide value will easily make sense in the conceptual sense. However, upon evaluating an asset at a deeper level of detail, understanding the value of an asset is not straightforward, especially from the standpoint of an early-stage innovator.

Value is an objective to maximize based on a selected criterion, which is usually a financial objective such as expected net present value (eNPV). Definitions of value

point to the ratio between risk-adjusted returns and cost. Value as a measurement has the special ability to align all relevant stakeholders around a common objective (value maximization), encouraging and supporting the creation of sustainable value.

Value is the best performance measurement tool because of its capacity to provide complete information. Establishing the value of a drug development program will take into account risk in terms of the Probability of Technical Success (PoTS), costs, and expected returns. These three elements will provide a complete picture of the of value creation process.

Early Value Assessment provides the needed critical information to support funding negotiations. It is the main task of the early-stage innovator to convince investors that the asset has the potential to succeed in a value-based world.

Typical questions to predict if research will be transformative

As mentioned before, early value assessment requires expertise and a multidisciplinary approach to be able to demonstrate real value in advance. Some challenging questions to answer are:

- 

How to improve the probability of success of your asset?
- 

How to predict drug differentiation at early stage using published data from relevant comparators?
- 

What is the optimal indication sequence strategy for your asset?
- 

How to better inform effective clinical development programs and trials designs?
- 

What is the justifiable price range for your asset to be cost-effective against relevant comparators?
- 

How to better inform forecasting- and valuation models with reliable data and assumptions?
- 

What are the key value drivers influencing the value story of your asset?
- 

What is the market landscape your asset will enter and how will your asset provide value?
- 

How to leverage your proprietary data with data from analogs to produce more reliable predictions?

Early value assessment: predicting future value under uncertainty



Early value assessment is a tricky exercise. It can be considered an optimization process, intended to increase the PoTS as the greatest challenge and opportunity for pharmaceutical R&D. Development programs predicted to reduce Phase II and III attrition will have a direct impact for improving R&D efficiency and reducing the costs per candidate. This, of course, will increase the value of the early-stage assets.

Producing development programs with the ability to secure superior outcomes in the treated population of patients will determine competitive differentiation and sustainable advantage for the early-stage asset.

Predicted development programs should contain convincing strategies on how the drug candidate can be differentiated by improving patient segmentation and diagnostic criteria, as well as its potential use as part of bundled service offerings that are better than the current standard of care.

The outcome of this exercise factors in the consequence of the indication sequencing strategy, and the trade-off of clinical development strategies and design options.

The nuts and bolts of early value assessment

The approach to early value assessment includes four stages. These four stages should provide a comprehensive analysis of the landscape the asset will enter, the needed value inputs for the forecasting and valuation models, and the price tag to negotiate with potential investors or partners.



1. Understanding the purpose of the early value assessment

- Partnering vs. Out-licensing vs. Merger and Acquisition
- Single molecule vs. development platform
- Perception of value by the potential investor (how value synergies would be created)



2. Primary & secondary research to understand the market that the asset will enter

- Disease area (epidemiology, severity, burden of the disease, disease management and specific guidelines, unmet needs, resource utilization, ...)
- Practice (treatment pathways, diagnostics, place of treatment, etc.)
- Market (sales in value and volume per indication and per product)
- Competitive environment
- Review of previous HTAs
- Stakeholder mapping in the selected countries
- Identifying relevant clinical outcomes, health related quality of life and patient report outcome (HRQOL & PRO) instruments per potential indication
- Coverage policy analysis
- External validation of results



3. Predictive modelling and simulation

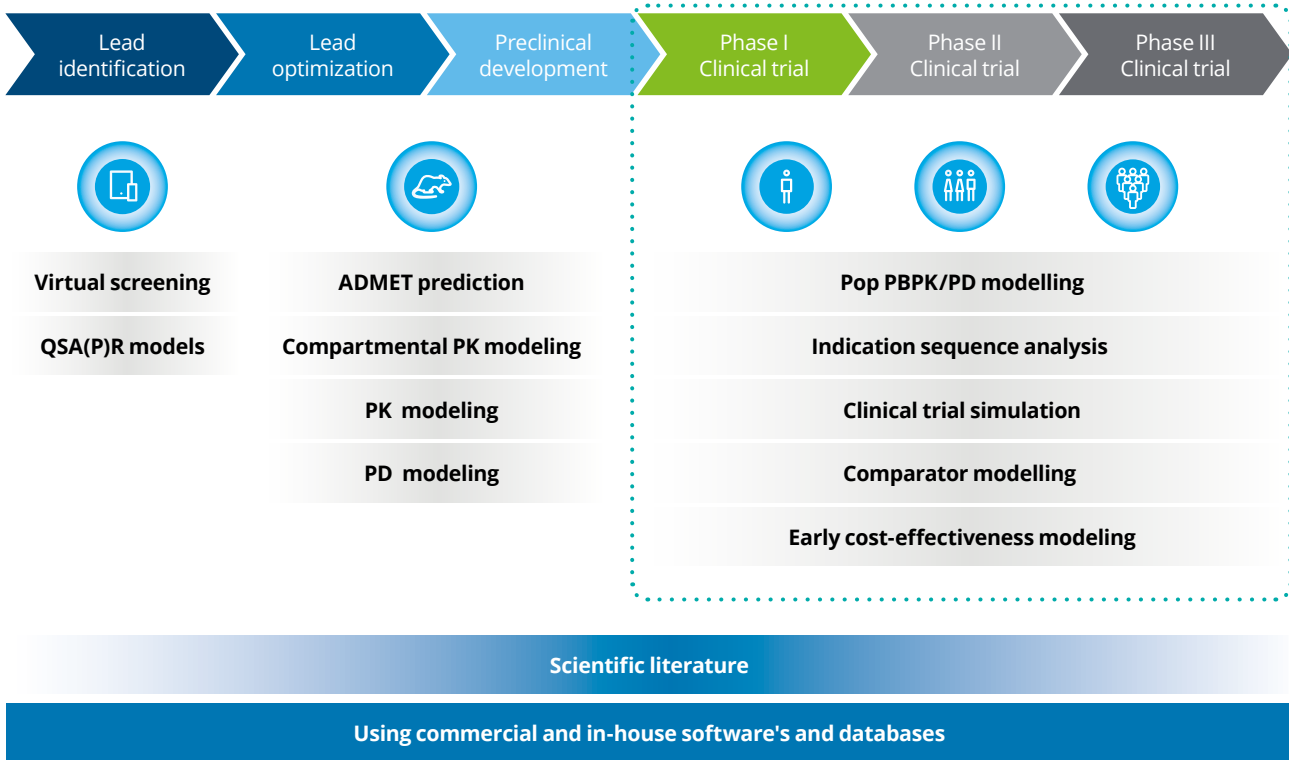
- Comparator modelling for product differentiation
- Early health economic modelling to assess early justifiable price and value drivers
- Indication sequencing analysis
- Scenario analysis to optimize PoTS



4. Forecasting and valuation modelling

- Leveraging previous gathered information to produce a forecast model in order to explore asset potential
- Generate a valuation model in terms of eNPV to capture costs, return and PoTS
- Final comprehensive valuation report

Figure 2: Model-driven early value assessment



Three main components of the early value assessment

- 1.** Cost of the development programs to advance the candidate through the different stages of drug development until market adoption.
- 2.** Expected revenues in terms of discounted cash flows and based on factors like pricing, market size, expected market shares, duration of treatment, compliance, competitor response and exclusivity.
- 3.** Risk, or inversely, the PoTS of a drug development program, meaning the probabilities of progressing from one stage to another over the course of drug development: early discovery, clinical development phases, regulatory approval, product launch, and commercialization.



Challenges related to a reliable estimate of an early-stage asset.

In most analyses, PoTS is treated as fixed, but PoTS is rather a consequence of the indication sequencing strategy and the trade-offs of clinical development strategies and design options. To compound the problem, several publications have analyzed historic PoTS in the pharmaceutical industry with significant

difference in conclusions. This has led analysts working on early value assessment models to be careful about which set of assumptions to use. Depending on the profile of the drug, there can be as much as 280% difference in value under different sets of assumptions.

Table 1: Overall Probability of Success from Eight Major Publications and their Probability of Success Ranges for 1993 to 2015

Studies	Phase I to Phase II	Phase II to Phase III	Phase III to Registration	Registration to Approval	Overall
DiMasi, 2010	71%	45%	64%	93%	13,4%
Paul, 2010	54%	34%	70%	91%	11,7%
Hay, 2014	64,5%	32,4%	60,1%	83,2%	10,4%
Smietana, 2015	56%	30%	59%	84%	8,3%
DiMasi, 2016	59,5%	35,5%	62%	90,4%	11,6%
Smietana, 2016	56,3%	37,5%	67%	93,1%	13,2%
Thomas, 2016	63,2%	30,7%	58,1%	85,3%	9,6%
Wong, 2018	66,4%	58,3%	59%		13,8%
Average	61,4%	37,9%	62,4%	88,6%	11,5%

Another challenge is to estimate a reliable value-based price corridor for the asset depending on the selected indication. Early health economic modelling can help overcoming this issue by providing a framework to compare the asset with relevant comparators using preclinical data or data from analogs. An early economic model has also the ability to clearly identify value drivers, in order to better define value-creating development programs to collect required evidence.

Tools of the trade

Model & Simulation techniques are very valuable to inform early value assessments. It integrates pharmacometric- and early pharmacoeconomic models to make the most use of available data, increasing data quality and allowing more reliable predictions. Results

of these models inform forecasting- and expected net present value (eNPV) models to produce reliable price tags. This model-informed approach provides an unbiased and data-driven price tag for the early-stage asset.

Table 2: Tools of the trade - Modeling and Simulation

Pharmacometrics	Pharmacoeconomics	Decision modelling	Other modelling services
<ul style="list-style-type: none"> • Non-Compartmental Analysis (NCA) • (Population) Pharmacokinetic/ Pharmacodynamic (PK/PD) • Physiologically-based PK (PBPK) • Model-based Meta-analysis (MBMA) • Clinical Trial Simulations • Disease Modelling 	<ul style="list-style-type: none"> • Cost-effectiveness Analysis • Cost-utility Analysis • Cost-minimization Analysis • Cost-benefit Analysis • Cost of Illness Analysis • Real World Evidence (RWE) 	<ul style="list-style-type: none"> • Decision trees • Markov Models • Discrete Event Simulations • Dynamic Transmission • Partitioned Survival Models • Multiple Objective Decision Analysis (MODA) • Multi-criteria decision analysis 	<ul style="list-style-type: none"> • Survival Analysis, multivariate regression, utility data analysis, etc • Value-based pricing • Cost calculators and interactive models • Probabilistic models • Bayesian approach • Time and Motion studies • Conjoint Analysis • Tiem-Driven Activity Based Costing (TDABC)



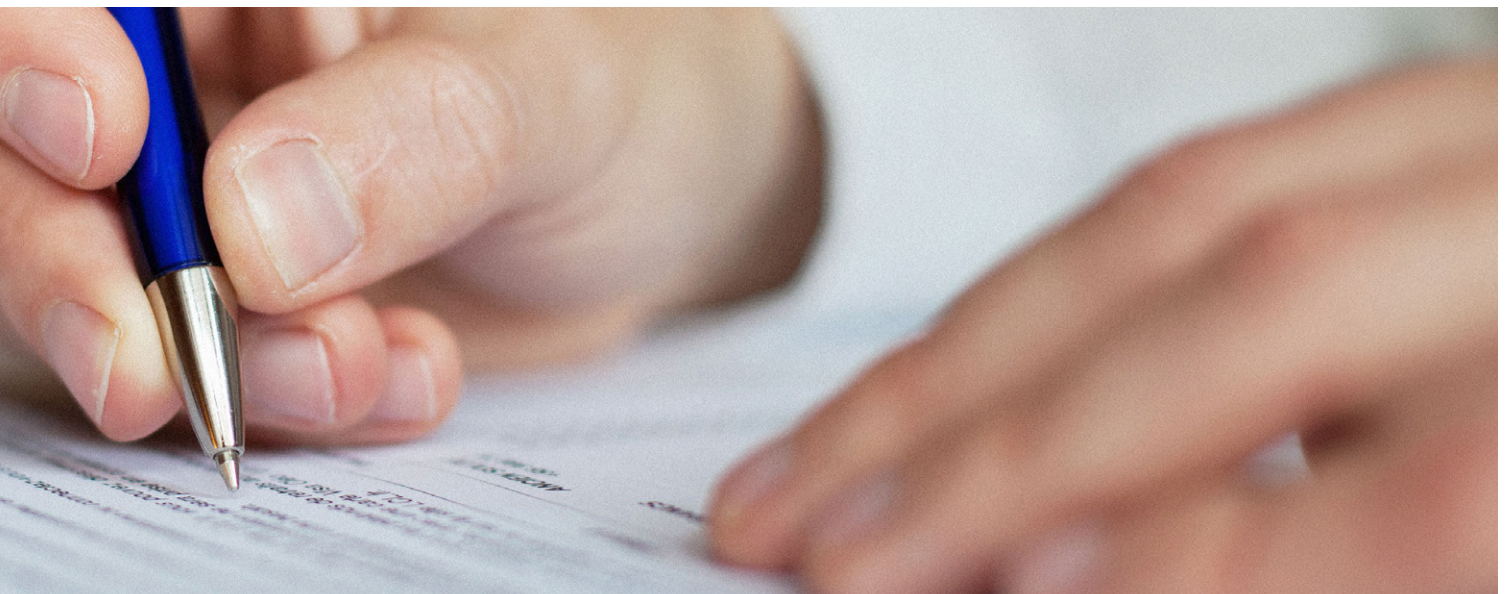
Benefits of early value assessments

Early stage innovators rely on early value assessments to evaluate the upside potential value of their assets to advance investor's interest.

Some of the benefits related to this approach are:

- Make the most use of available data, increasing data quality and allowing more reliable predictions
- Increase the probabilities of technical success
- Integrate a value-based approach to support your value story
- Define the real value of your asset to convince potential investors
- Align your organization on what really matters to support future launch activities
- Reduce uncertainty regarding the data and assumptions informing forecasting- and valuation models
- Integrate a data-driven approach to your decision making process to reduce human cognitive biases

Deloitte's HEOR & Market Access team provides Biopharmaceutical companies with highly specialized modelling and simulation services in a modular approach. We help your organization make complex decisions across the lengthy, risky and costly drug development process in a transparent and quantitative manner. We offer an integrated approach connecting physicochemical, in-vitro, ADMET properties, disease model information, population analysis and early economic evaluations in an envelope of mathematical modelling with a clear emphasis on successful clinical development and commercialization.



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