AESTIMO INSIGHTS

A Novel Valuation Model For Healthcare Technologies Development

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Executive Summary

In healthcare the development process of a new medicine takes many years and is very costly. About 90% of all medicines that start being tested in people don't reach the market because they are unsafe or ineffective.

For entities with strategies of licensing their innovations to larger stakeholders for downstream development this means that significant risk has to be carried for a long duration before knowing whether the product was worth the investment. Additional risk is incurred upon market release because regulatory approval alone does not guarantee nor is linked to reimbursement and revenue generation to enable developers to obtain acceptable rate of return.

Pharmaceutical research and development (R&D) returns have declined to <2% in 2018, down from >10% in 2010.

These risks can be reduced with the correct integration of healthcare marketplace realities with optimisation and innovation of the total development pathway.

Extensive research and real market simulations performed by ourselves has indicated integrating a more comprehensive source of data in decision making not only provides real value but also enables augmented and more accurate valuations, which when matched with real market need, reimbursement potential and strategies to increase application potential can compensate for lower return of investments (ROIs).

Leveraging over 45 years of global experience maximizing value from healthcare innovations

INTRODUCTION

In healthcare the development process of a new medicine takes many years and is can cost over US$ 2 billions. Of all medicines that start being tested in humans about 90% don't reach the market because they are unsafe or ineffective (Link). This means that significant risk has to be carried for a long duration before knowing whether the product was worth the investment.

Additional risk is incurred, because regulatory approval alone does not guarantee reimbursement by payers and thus revenue generation.

Concerns regarding the growing gap between demand for health services and technologies and available resources has long created the need to regulate healthcare expenditure and governments have increasingly introduced formal systems to assess the value for money of health care technologies coming to market. The predominant processes to do so are Health Technology Assessments (HTAs).

The introduction of the National Institute for Health and Care Excellence (NICE) in 1999 in England significantly contributed to the globalisation of HTAs. Nearly every country has now HTA authorities in place.

Value assessments conducted by these authorities consist of compiling and analysing the evidence to show the health and economic benefits of a product compared to the standard of care are sufficient to justify the price desired beyond the requirements of regulatory marketing authorisation authorities.

Delays in reimbursement decision-making can lead to substantial delays in a new product gaining market access. Negative reimbursement decisions by payers however will hinder market access substantially. Delays in reimbursement or negative reimbursement decisions will hinder and even prohibit sales and return on investment.

Achieving reimbursement and market access requires meeting the evidence needs of payers and HTA organisations. For each product this has to start early (Phase 2 trial planning the latest) in and throughout the development process in order to optimise the chances of gaining market access at the desired price for the desired / full licensed population which will increase market relevance and further unlock ROI.

Pharmaceutical R&D returns have declined from >10% in 2010 to <2% in 2018 (Link)

These risks can be reduced with correct integration of healthcare marketplace realities with optimisation and innovation of the total development pathway.

For every health focused entrepreneurial venture, a positive risk adjusted net present value (rNPV) calculation on any product in development is the accepted metric that upon market release, the financial return will exceed the cumulative life cycle costs of research, development, market validation, market access, market release, manufacture and sales and therefore potentially justify the initial outlay, i.e. ROI.

Our own insights and research have shown that there is a serious disconnect of value perceptions, risk understanding, expectations, knowledge and value generation between stakeholders at the different ends of the development pathway, that has serious consequences for when a company attempts to out-license its product to a larger company or attempts to commercialise a product.

There are multiple reasons for this:

1. The definition of the terminal market value in the rNPV equation, in which global or Total Accessible Market (TAM) values are used instead of more relevant SAM and SOM values [SAM (geography differentiated market value) and Serviceable Obtainable Market (SOM (percent of market penetrance that can be achieved within a serviceable accessible market,)]; launching a healthcare technology in different 'regulatory' jurisdictions (North America, Europe, Asia-Pacific, Mercosur, and potential further geographic distinctions) cannot occur without satisfying the local clinical requirements which cannot be geographically transferred.

2. The pertinence of HTAs including comparative effectiveness, affordability and cost-effectiveness evaluations comparing the new intervention to existing standards of care in that SOM to define whether, where and at what price the product will be reimbursed. While valuations simplify global market values, the geographic diversity of HTAs and if, how and for what decisions are made means local geography valuations have to be used.

3. The complexity and volume of clinical data that needs to be generated managed and continually collected to generate a high-quality reimbursement argument with associated costs.

4. The use of generic/total market probabilities of clinical transition of a therapeutic.

5. The perception that total indicated sales represents the terminal market value to be used, ignoring the reality that nearly two thirds of the sales costs are used to manufacture and sell the final product.

Many companies still have incomplete perspectives of the full market chain and pharmaceutical marketplace, especially in the link between regulatory approval and reimbursement and what the priorities of larger entities are and the resulting commercial potential of a product. The general understanding is that the three are synonymous, when in reality they are not.

HTA authorities operate within a network of other healthcare stakeholders that, together, determine whether a medicine is allowed to enter a market, who receives the medicine, and who pays for it. Regulatory authorities are responsible for assessing drugs on their efficacy and safety. Approval is required from these agencies to receive market authorisation. National, regional and, in some jurisdictions, sub-national organisations then negotiate with the manufacturer on drug price, reimbursement status (as in specifically for what based on evidence-based medicine) and allocated funding."

The value driver, therefore, is integrating these three, and reverse engineering back through the value chain to the earliest stage possible, to ensure all design and implementation systems address the final needs, including identification of additional areas of application, that can significantly boost the final value of the product.

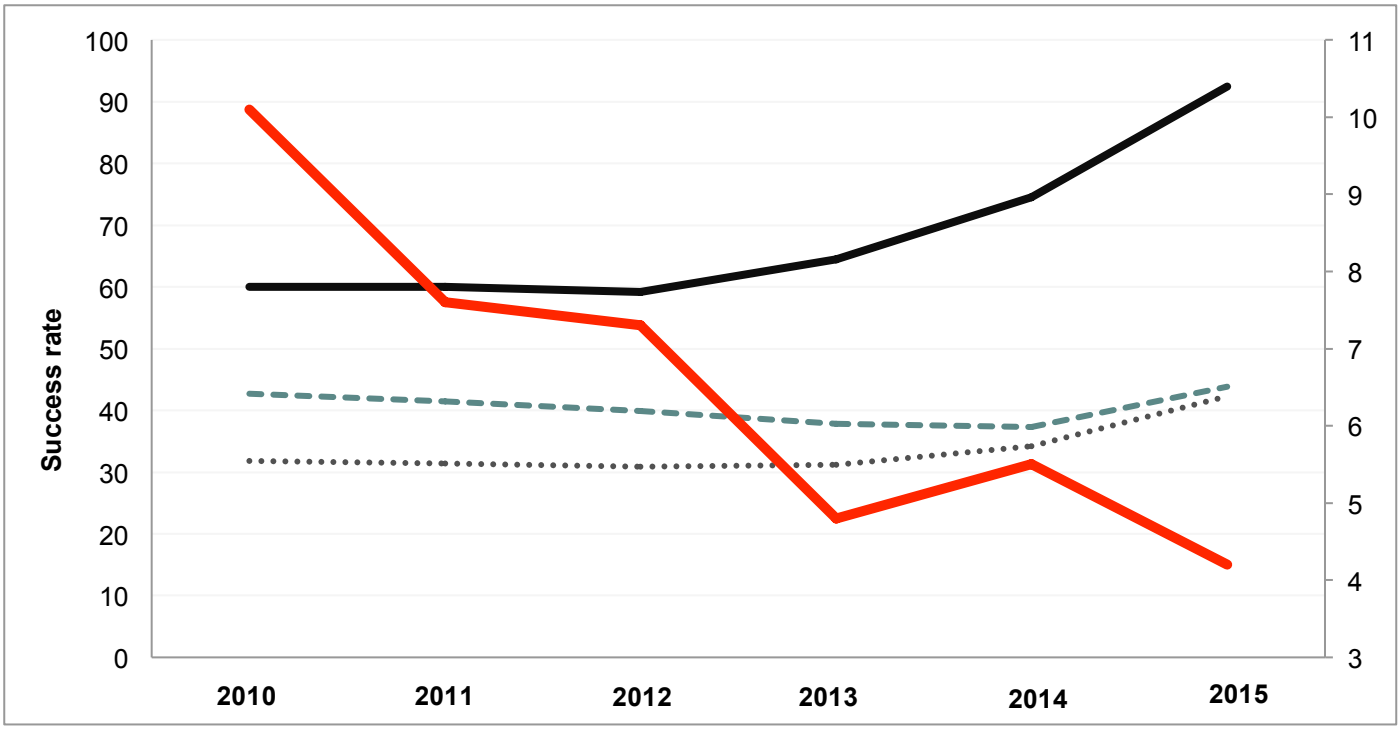
We therefore developed a novel valuation model for health care technologies including the above points.

The model

We used the industry standardized valuation model and equations for performing rNPV calculations (Link.).

We integrated full development costs into the rNPV calculation, followed by indication specific regulatory (Link) and HTA success rates (data on file) obtained from recent analyses published market size values for the complete drug development lifecycle. Differing terminal market values were based upon level of market penetrance of existing standards of care for the different conditions, against which any new intervention would be compared for reimbursement purposes. This enabled us to model stage of development specific rNPV calculations as a level of 'arguable-competitiveness to existing standard of care' of the product.

Clinical trial success rates, despite having increased, do not increase the long-term ROI



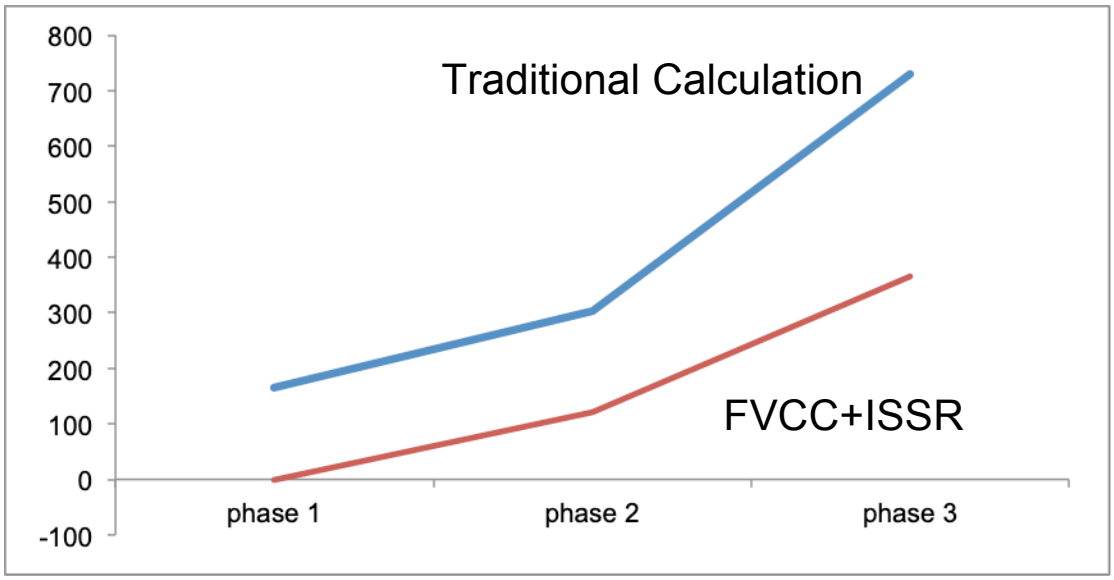
Innovations are being greatly overvalued

Combining the full value chain costs (FVCC) and indication specific success rates (ISSR) provides significantly reduced but more accurate rNPVs of clinical stage therapeutics during their development.

CARDIOVASCULAR INTERVENTION

(based on expected future sales of a $USD 25 Bn TAM)

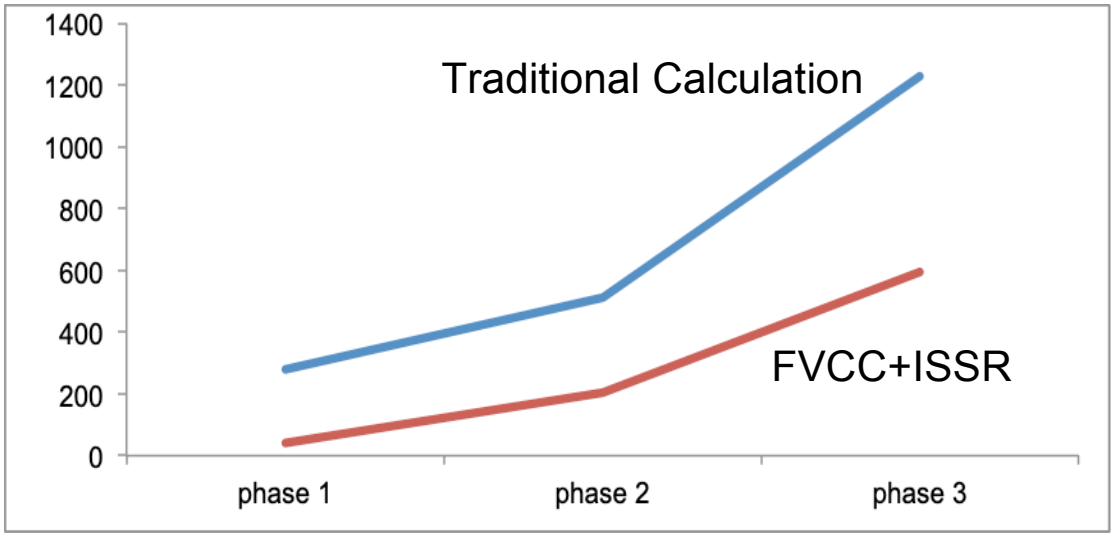
rNPV in $USD Mn



DIABETIC INTERVENTION

(based on expected future sales of a $USD 30 Bn TAM)

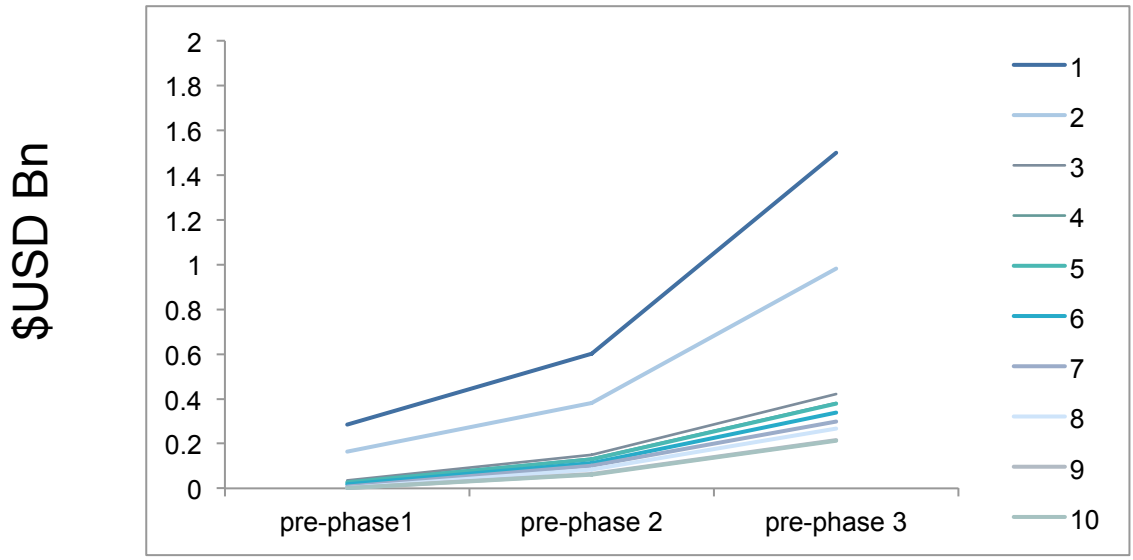
rNPV in $USD Mn



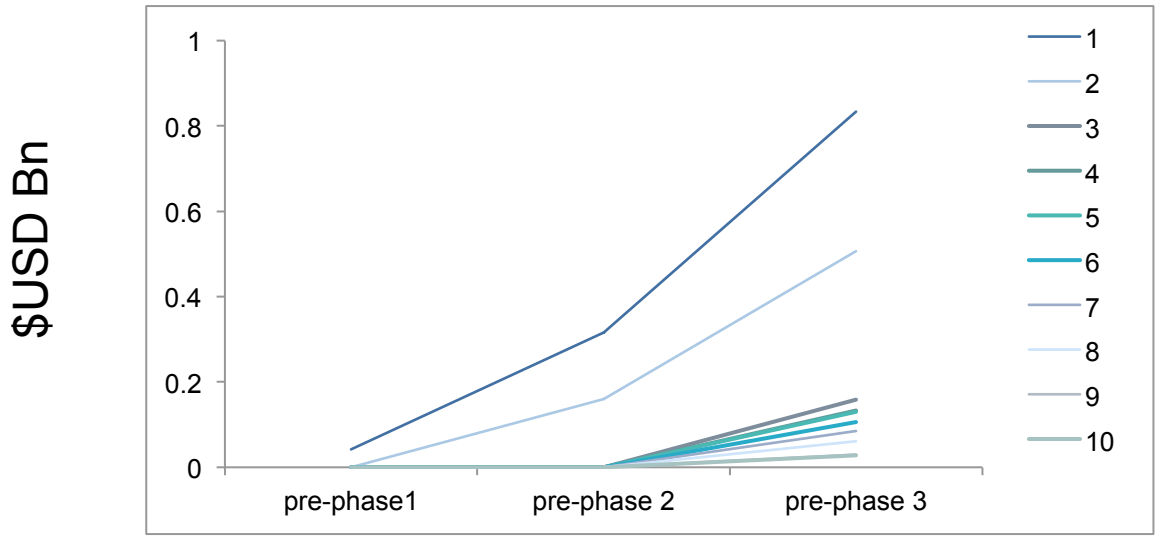
HTA and reimbursement decisions are not being integrated into risk

Being responsible for a start-up/small company or the head of a sub section of a business unit in a mid sized pharma with an innovation which can address a major medical need in cardiovascular disease, you plan to license it to a larger stakeholder because you do not have the funds necessary to move it to market release. You need to convince an external investor or the finance committee to agree to finance the development. The top ten selling drugs in that indication, over their protected lifetime in the past 12 years have generated just over $USD 180 Bn in revenue globally, with the best selling drug having 30% of the market, the second best 20% of the market, the next four best drugs at 11% and the remaining hovering around 7% of the market; the mid four could only reach profits of around $USD 100 Mn, while the latter could only just make a ROI if global sales were obtained and all development was performed in-house.

Traditional rNPV calculation: reverse engineered for top 10 CVD drugs

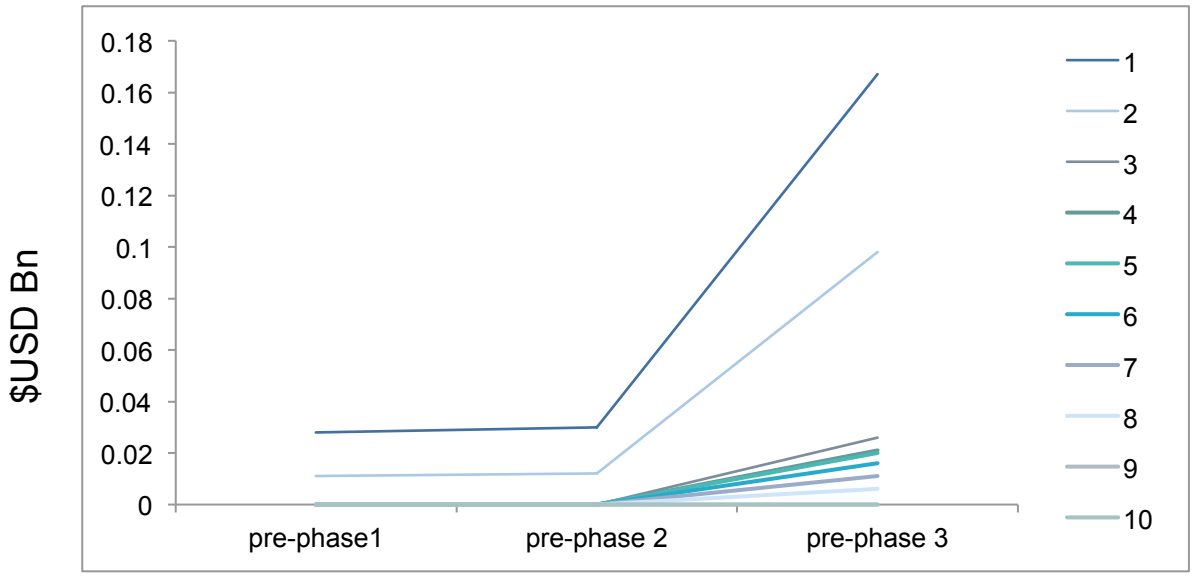


FVCC+ISSR rNPV calculation: reverse engineered for top 10 CVD drugs



As revenue does not account for the sales and manufacturing costs associated with the product (60% of revenue), to have a better understanding to know if your innovation will actually impact the bottom line, the terminal market value you should include accounts for this reduction, and to assess your innovations potential market relevance you reverse engineer the rNPVs of the top ten selling drugs to assess where your innovations global competitiveness stands.

PD-DRR © model rNPV calculation: reverse engineered for top 10 CVD drugs



Even when accounting for full value chain costs and the indication specific success rates, the profit-generating threshold of your innovation is still too high, i.e. your innovation needs to be either close to best-in-class, and/or already successfully passed through expensive later stage clinical testing to be of interest to larger stakeholders: it simply carries too much market risk. Additionally, it is not incorporating the risks associated with the reimbursement decision-making bodies located within your global markets, which have different criteria (regulatory and market based which determine which determine which interventions they will pay for).

The probability of 'not reaching' the reimbursable product market are 94% from pre- phase 1, 88% from pre-phase 2, and 70% from pre-phase 3 (the 10% success rate from preclinical to regulatory approval does not account for full reimbursement agreement which only occurs on average 56% of the time).

This has led us to generate a new version of rNPV valuations that integrates in this changing market dynamic into the risk value, matched with full costs and indication specific success rates. As the innovation moves up the value chain and gets closer to market, it becomes more sensitive to information (external and internally) which defines its future reimbursement value, termed Progress Dependent – Dynamic Risk Rate modeling, abbreviated to PD-DRR ©. These factors, based upon our prior experience, can and also should be integrated into early stage decision making to prioritise those innovations that should be funded, and what actions should be taken during this process, so that when the innovation enters clinical studies, success rates are increased and revenue potential maximised.

Using this model, the rNPVs are much lower, which enables you to perform a more stringent triage of your pipeline. The implication is that PD-DRR is used throughout the innovation development to make sure it is always aiming towards maximum revenue generation. This is achieved by integrating in market and patient dynamics, and reimbursement based criteria (locally and globally) into your development implementation plan; the capacity to move your innovation into the global market becomes clearer, further increasing its value and attractiveness to all potential customers.

MAXIMISING VALUE

Our research and real market simulations performed have indicated integrating the following perspectives in decision-making not only provides real values, but also enables enhanced valuations:

- Use of a more accurate risk rate, indication specific success rates and correct full economic costing in valuations provides a far more accurate stage specific valuation of a product as a function of its actual revenue generating potential
- Use of SOM to define initial valuations, matched with implementable strategies to increase market penetration in SAM and obtain market penetration possibilities in the TAM enables higher valuations and better market opportunities.
- Reverse engineering from the actual market place, through the HTA process, how clinical data is generated for use in HTAs and how this is directly impacted by early stage decisions indicates whether an innovation has real potential to be of value to downstream stakeholders.
- Use of HTA data requirements to define and design innovation processes in the early stages enables better de-risking throughout the pathway that reduces costs but increases value.
- Assessment of successful revenue generating products and the strategic actions taken to realise their values, when matched with effective streamlined and high-quality constraint-based decision making, can be used to:
    - Identify which innovations should be developed
    - How they should be developed
    - Define strategies to obtain maximum value from them

  In combination with our highly accurate valuation approach, this will reduce capital wastage, increase global market penetrance and address real market need to generate higher value innovations, which are of greater interest and relevance to key stakeholders

What next ?

Our work indicates that all stakeholders need to take a holistic approach to valuation to de-risk development programmes and pipelines. This will facilitate improved decision making, better therapies, higher chances to get payers to pay the desired price for the whole licensed population resulting in a better return of investment than currently.

While modelled for medical intervention development, the outcomes of this work can also be applied for evaluation of diagnostics and medical devices, and we are also exploring other regulated sectors.

We are in the process of launching our model as part of a fully integrated solutions portfolio to enable the potential to increase return of investment and deliver much wider benefits to investors, developers of healthcare technologies, business valuation entities, charitable organisations and governments.

PD-DRR ©

HTA & reimbursement integrated valuations linked into early stage innovation design, that can applied for all interventions, throughout the total value chain, leveraging complete and realistic market potentials to generate maximum benefit for all stakeholders

- **Each PD-DRR calculation, with implementation design and follow up, incorporates data inputs specific to the indication, type of intervention, market size and location, clinical trial structure, and outcome measures as relevant to reimbursement decisions.**
- **Value is only created by combining increased development success rates with maximised revenue generating plans for the innovation throughout development.**
- **Account for market generated risk fluctuations**
- **Make more stringent go/no-go decisions**
- **Identify real Global market relevance; and Global market values**
- **Prioritise innovations with maximum value and implementation strategies to achieve it**

About the Authors

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Jonathan is an International Portfolio/Contract Manager with 22 years global experience, working with all stakeholders in early stage intervention design and development. He has managed over €600 million in R&D funding in global innovation healthcare projects, co-founded several hi tech start up's and innovation consultancy firms. Since 2010 he also runs Echino Ltd, an innovation management company specialised in international partnering, development and ecosystem design. Ecosystem design has been performed for many global partnerships focusing on common and rare diseases as well as complex convergent technologies.

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Maximilian is a health economist with over a decade experience in the pharmaceutical industry (Global, regional, UK / Ireland). He has worked on a wide range of disease areas from very common to very rare conditions including some of the world's largest selling pharmaceutical products (Humira, Enbrel, Plavix, Yervoy, Abilify as well as many others). He has accumulated a broad depth of insights on identifying and generating value having worked on over 150 HTAs. Since 2016 he also runs Athena Market Access Solutions Ltd., providing pricing and market access solutions to organisations in the life sciences industry.