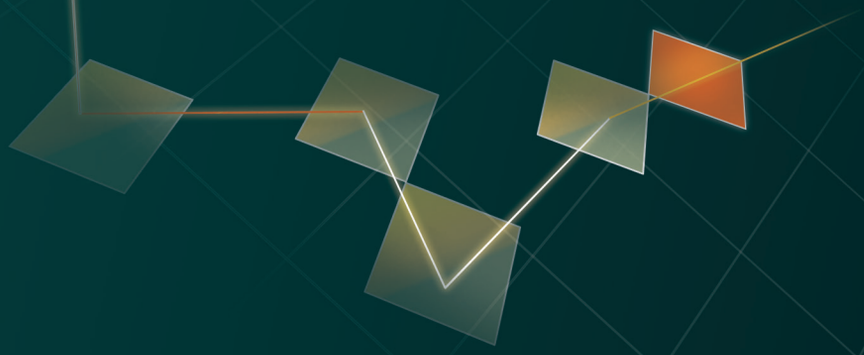
Strategy Foresight

Decision Support for the 21st century

Disentangling the Complexities of Health Technology Assessment.

Identifying the most optimum route for market access and pricing.



"The risks of the future are unlikely to come from the precise places that they've come in the past. In a rapidly evolving system new risks can develop out of things that don't appear initially, that don't appear to contain that kind of possibility"

Jack Lew, the former US Treasury secretary and an advisor to Barack Obama, 2017

As a global industry, the challenge for pharma is that it not only needs to create clinical trials for several regulators over a 12-15 year period, but it must also develop new Market Access and Pricing models to convince Health Technology Agencies into accepting its products.

Create new Market Access and Pricing models

In an era of austerity and increasing complexity, the ability of senior executives to conceive or adapt a market access and pricing strategy and implement it, whilst it remains relevant, is becoming increasingly difficult to achieve. The real challenge is for an executive team to be able to maximise the length of time it must consider its situation before applying solutions to exploit opportunities or to avoid threats or unintended consequences.

Avoid threats or unintended consequences.

In this article, we highlight the issues facing senior management and present our proprietary Fibonacci Decision Support toolkit as a new way of maximising the value of clinical-stage drug candidates.

About the Author

Dr David Campbell has spent the last 25 years working across the pharmaceutical sector. Initially as an academic, David spent several years support early stage research organisations at SmithKline Beecham and then GSK implement new technology and improve decision making. Following a successful career in the industry David continued to support the industry as a senior advisor to mid-cap and large-cap pharmaceutical organisation on corporate strategy, portfolio management, commercialstrategy and business development and licensing.

Today, David works more closely with younger, start-up life science organisations across the UK and Europe.

David is non-executive Chairman of Strategy Foresight

The Maelstrom of Market Access and Pricing

Healthcare affordability and the value of pharmaceutical products is a 'wicked problem' where facts are uncertain, values in dispute, stakes high and decisions urgent. Mounting economic pressures and biotechnology advances have made market access and pricing the focus of a socio-political debate. Drug pricing regularly makes headlines, with patient advocacy organisations, medical communities and political leaders weighing into the discussions. Both government and private payers around the world have tightened coverage requirements as drug budgets cannot measure up to the increasing healthcare needs of an aging population. The mandate is that life sciences firms provide compelling evidence of both the health benefit (the value) and the financial impact (the affordability) of treatments and therapies. The question is how do you select a therapeutic modality for development on its promise to pay in an ever-changing and cost-constrained world?

Contextual environment						
Drug	**Development phase**	**Burden of disease**	**Comparator**	**Real World Evidence**	**Environment**	**Affordability**
Our drug candidate	Discovery	**Well-defined population with low co-morbidities**	Well-defined gold standard	Compelling	**Guidelines in place to accept new therapeutic approach**	Cost-effective established
Competitor A	Pre-clinical	Well-defined population high co-morbidities	**Sub-optimal standard**	Strong	Society willing to accept new approach	Cost-effective being determined
Competitor B	Phase 1	Heterogenous population with low co-morbidities	No standard exists	**Moderate (data being generated)**	Healthcare system aligned to current approach	**Not cost-effective therapy**
———	Phase 2	Heterogenous population with high co-morbidities	———	Weak to none	Guidelines required before broad adoption	———
———	**Phase 3**	———	———	———	———	———

Figure 1: An advanced strategy table illustrating the internal (affordability) and external (value) considerations driving the selection of a New Chemical or Biological Entity. Through the process of algorithmic filtering, the vast number of possible combinations can be easily reduced to a few combinatorial strings identifying which ones are viable and worthy of further analysis. This is achieved by assessing each

Complexity and uncertainty of the landscape

The challenge of negotiating separately with the various Health Technology Assessment Agencies in EU and Pharmacy Benefit Managers in the US, adds to the complexity and uncertainty of which economical clinical candidates to pursue. Within each country, further fragmentation is found regionally – the UK alone has over 200 Care Commissioning Groups who can choose to ignore NICE recommendations. The question for senior executives is therefore, given the long-term frame horizon in pharmaceutical development, how do you identify an innovative clinical treatment given all the uncertainties not least what would be the standard of care 5-10 years down the line? The figure below illustrates the sheer size of the challenge – some 175 million unique scenarios in a 14-dimensional space. Which one(s) do you go for?

		Strategy space				
Combinations	**Reimbursement**	**Time**	**Major EU market**	**Innovation as defined by HTA**	**Likely HTA Outcome**	**Decision**
Expect use with gold standard	Full cost reimbursable - premium	**Within 2 years**	**UK**	**Major**	Recommended	**Go it alone Partner**
Expect use with another novel in combo	Full cost reimbursable - reference price	Between 2-5 years	France	Important	**Optimised**	Out-license
Monotherapy	**Risk-sharing (rebate) / payment-by-results**	More than 5 years	Germany	Moderate	Not recommended	In-license
———	Cost-sharing (discount)	———	Italy	Minor	———	Terminate
———	Unlikely to be reimbursable	———	Spain	None	———	———

pair of cells in the entire matrix for logical compatibility given the data which is available at the time. The example shown refers to an orphan medicine (see Box 1 for case study) where red cells are input drivers and blue are outputs. The model can be driven from anywhere in the matrix. Other examples are available on request for a biosimilar and an oncology product.

Box 1. Therapy X, an orphan medicine, is substantially likely to improve the quality of life in patients with no other therapy options and will be priced at Đ50,000 per course. The available information is as follows :

- Population defined by genetic testing and physician assessment
- No licensed treatments currently available for the patient population. 95% of patients incapacitated by 30 years of age. Current standard of care only effective in 5% of affected patients
- Political pressure to support patient populations with greatest unmet need
- Minimal budget impact due to small patient population (3/100,000 in Europe). However, high net price per treatment and therefore not cost-effective when assessed under conventional cost-utility reimbursement thresholds (e.g. NICE threshold in UK)
- Single-arm study due to ethical considerations of inefficacious standard of care comparator and lack of historical comparators
- 20% reduction in the proportion of patients incapacitated by 30 years of age

[1] Dunlop, William C. N. et al. "BEACON: A Summary Framework to Overcome Potential Reimbursement Hurdles." Pharmacoeconomics 34.10 (2016): 1051-1065

Differences between HTA bodies imposes a set of diverse rules

Paying for pharmaceutical products varies from country to country. The cost-effectiveness following scientific approval is not harmonized in Europe let alone the top EU5 countries. For example:

- Apart from NICE in England and the Scottish Medicines Consortium recommending against access regardless of MHRA regulatory approval for many medicines, the Capped Expenditure Process is a sign of times to come. Launched by NHS England and NHS Improvement in April 2017 to ensure rapid improvement in the financial performance of health regions with the largest overspend, a new 'budget impact threshold' of £20 million per year has been introduced to better manage the introduction of new treatments deemed cost effective, but costly.
- In France, a new regulatory body, the National Agency for the Safety of Medicines and Health care Products requires data from active comparator trials. Products will be awarded an

ASMR and an SMR rating; ASMR 4 (parity) or ASMR 5 (EU reference pricing) would mean no price premium versus existing products.

- Under AMNOG, the process in Germany has become challenging with few companies emerging with positive results. Bayer/Regeneron's eye drug Eylea, given the green light by NICE, was initially rejected by IQWiG.

- The process in Spain is split across three levels (national, regional, and local). A formal requirement for cost-effectiveness has been introduced at the national level; highly innovative, expensive drugs are increasingly assessed at the regional level.

- In Italy, the role of pharmacoeconomic studies at both national and local levels is be coming clearer and more important with over 100 cost-sharing agreements refunding $200 million per year since 2013.

A Systematic Approach to Predicting the Reimbursement of Early-Stage Drug Candidates

Over the last 10 years the team at Strategy Foresight have developed the Fibonacci Decision Support Framework. Used today by several organisations including those in the defence industry, the framework provides a tested approach to mitigate uncertainty and facilitate decision making in a complex environment.

By incorporating this approach into Market Access and Pricing decision making, companies can:

1. Define a model to better understand the complexity and structure of the market access of early-stage drug development candidates.

2. Understand the interdependencies of key outcomes of market access and reim bursement options from the viewpoint of payers, providers and patients.

3. Develop a system by which key clinical and commercial factors can be combined to unearth feasible scenarios and associated strategies. We have seen that by following these simple steps and sharing the real-time dynamic models organisations can establish practices to dramatically improve the performance of their early-stage research operations.

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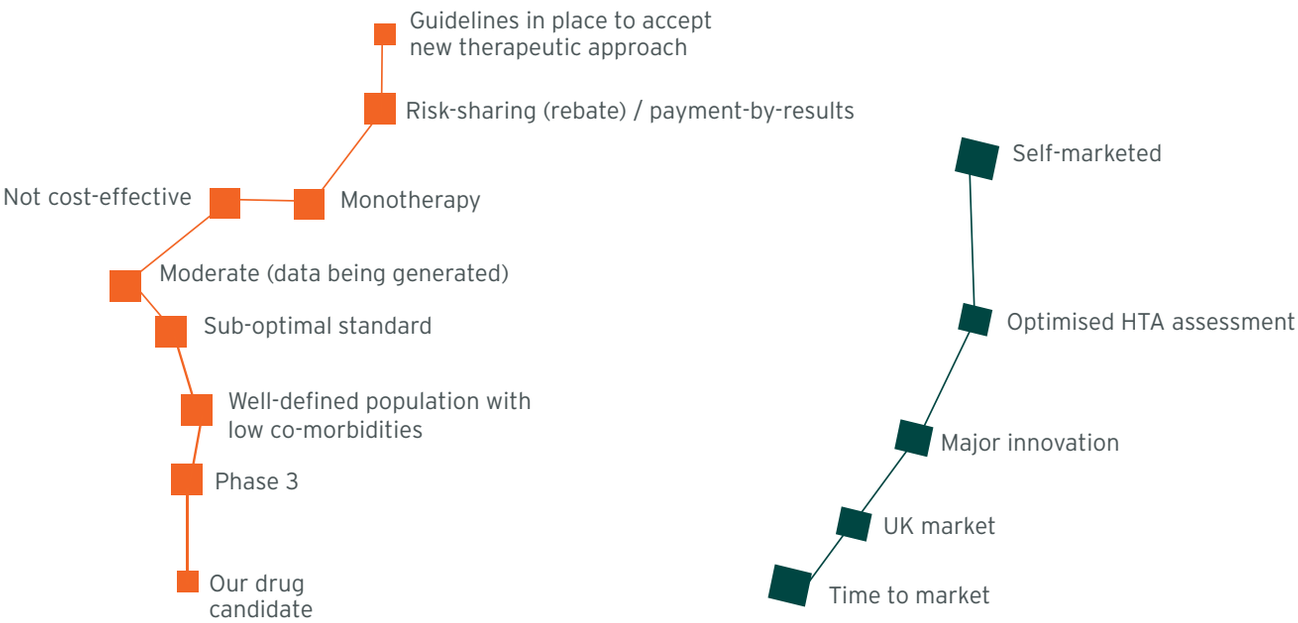
Unearthing key critical pathways from a range of possibilities

Linking pre-market contextual environment with strategic execution



Living through a period of "unusual level of uncertainty" *

Strategy Foresight helps decision makers to confront issues such as:

- How can I handle uncertainty and help mitigate strategic and operational risks?
- How do I get to grips with both internal and external operating environments impacted by high levels of uncertainty and complexity?
- What existential risks should I be aware of?
- How can I generate new viable solutions that will help improve performance?
- How do I keep my organisation agile in a "wicked" world?

*Ben Bernanke, the former chairman of the US Federal Reserve

The methods and processes
strategic option analysis

The methods and processes Strategy Foresight deploys, a form of "strategic options analysis", helps structure problems and support decision making, notably when they are complex, "wicked" and inherently contain high levels of uncertainty. It is particularly well suited in assisting decision making when addressing the inherent uncertainties and risks associated with early-stage investment strategy formulation. This acts as a "strategic insurance vehicle" to enhance management's ability to mitigate the investment risk under such circumstances. By systematically structuring and examining the total set of possible relationships in a multidimensional, usually non-quantifiable, problem space the software supported process enables the problem to be reduced to a much smaller set of viable options or solutions. This helps to reduce the chance that events will play out in a way that management has not previously imagined and considered.

Whilst developing innovative strategic choices, the dashboard displays in real time the elements of a decision including inputs, outcomes and goals, gives interactive options analysis, provides the user with an audit trail as decision validation, and crucially through its stakeholder representation, allows users to take ownership of the problem and outcomes

About Strategy Foresight Ltd –
Decision Support for the 21st Century

Strategy Foresight Ltd is a technology company that develops decision-support software solutions to help enterprises improve their decision making under conditions of uncertainty and complexity. The technology supports senior leadership tasked with a critical series of difficult-to-quantify, complex and interconnected problems.

The decision-support software platform combines qualitative and quantitative data into a single easy-to-use visually interactive tool. It is used by several major companies in the Life Science, Engineering and Defence sectors, NATO being one of clients. The software-assisted process enables possible alternative developments that are constructed using quantitative data as well as the experience and intuition of experts and stakeholders. Strategy Foresight helps decision makers to confront issues such as:

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Phone: Phone: +44 (0)77 03 132 751
E-Mail: info@strategyforesight.org