

Pharma Futures 4

Shared Value:

Rebuilding Pharma's Contract
with Society



Executive Summary

PharmaFutures4

The *PharmaFutures* series was created in 2003 to allow investors to hold a sustained dialogue with senior pharmaceutical managers about how they were seeing and responding to challenges in the external operating environment. The dialogues aim to validate the business case for adjusting the biopharmaceutical industry business model to more effectively balance changing market realities and societal expectations. At its heart, *PharmaFutures* seeks to enhance a business model that combines sustainable shareholder value and strong patient health outcomes. It aims to build trust and foster an environment in which collaborations and partnerships between industry and key stakeholders can flourish.

This report is a record of the fourth iteration of the *PharmaFutures* dialogue between pharmaceutical executives and institutional investors. The dialogues are now run by Meteos Ltd, a not for profit company formed specifically to seek cross sector collaborations to solve complex problems. Our investor dialogues are a supplementary research tool, which use direct dialogue between companies and their investors to generate new and original insights, in order to enhance strategic planning and investment decision-making.

Disclaimer:

As a multi-stakeholder and collaborative project, the findings, interpretations and conclusions expressed herein may not necessarily reflect the views of all members of the Working Group who took part in this project in their personal capacity. The report was compiled for information purposes only and it is not a promotional material in any respect. The material does not offer or solicit the purchase or sale of any financial instrument. The report is not intended to provide, and should not be relied on for, accounting, legal or tax advice or investment recommendations. Although based on information believed to be reliable, no guarantee can be given that it is accurate or complete.

Executive Summary

The biopharmaceutical industry¹ is vitally important to society, a fact that is reflected in the social contract between the industry and society that evolved after World War II. In exchange for developing safe, effective, affordable and innovative treatments for unmet medical need, society rewards the industry in the form of markets, intellectual property and market exclusivity for its products. The industry's social contract generally functioned to mutual satisfaction in the industrialised markets until the mid-1990s. Since then, concerns over increasing prices, intellectual property claims and access in the developing world have combined with increasingly complex science, costly regulatory requirements and changing payer behaviours to place the social contract under severe strain.

Despite this, the importance of the sector is growing as requirements for new treatments for the rapidly growing incidence of chronic diseases worldwide combine with the urgent need for new antimicrobials and therapies for neurodegenerative diseases, such as Parkinson's and Alzheimer's Disease, for an ageing population. The industry has unique skills to translate academic discovery and research into safe, effective products.

It has specific competencies for taking products through complex regulatory processes and it has a wealth of knowledge about disease states. It has a scale and reach that allow it to understand and respond to globalised disease trends. It is therefore in the interest of patients, regulators, health workers, health insurers, industry and shareholders to reframe relationships and make the social contract work again.

This report of discussions between the industry and its investors outlines two major challenges to the industry's ability to successfully develop treatments for unmet need. It analyses first the continuing challenge of R&D productivity and second the changes to how medicines are paid for. It then reviews the relationship between the two.

The R&D Challenge

Over the last ten years R&D expenditure has increased dramatically, whilst new medicine approvals have decreased and the mix of product approvals has shifted towards speciality drugs, many with lower commercial potential than earlier blockbusters. This has led

to a "productivity drought". Intense attempts by the industry to address this have led to an increase in the number of new drugs emerging from Phase 1 trials and many company pipelines look promising. Despite this, the attrition rate is higher now than it was ten years ago; meaning that the

probability of success is lower than it was previously. The R&D challenge is a multi-faceted problem that cannot be reduced to a single explanatory variable. However, the following five contributory factors have been particularly significant.

¹ This report covers the broad category of biopharmaceutical industry which includes both large pharmaceutical companies and the newer biotech companies.

Industrialisation

Traditional drug discovery in the 1950s and 1960s relied heavily on an understanding of animal physiology, strong pharmacology skills and labour-intensive chemistry. In the 1980s and 1990s the industry embraced new industrial techniques (e.g. automated drug libraries and high throughput screening) for drug discovery. In the process, the skills bias within the industry moved away from traditional pharmacology and physiology. Many chemists were replaced by machines and personnel budgets were instead spent on molecular biologists and bio-informaticians who were needed to help interpret the next wave of technology – genomics and new target discovery. This increasingly reductionist approach led to a loss of focus on integrated biology and experimental medicine, and an over-reliance on the belief that identifying the molecular target would be sufficient to produce a drug.

Duplication

Another result of the widespread application of industrial techniques was the evolution of a “shots on goal” mentality in which the number of things being worked on became a surrogate for their quality and validity. Once a target had generated useful data, the industry came to hunt as a pack, focusing on a relatively small number of validated targets. The result was the race to the finish line to launch significant improvements on the drugs that had been successfully launched as first in class pioneers. Some were indeed best in class but many proved to offer

only modest clinical differences.

The consequences of companies “working under the lamp post”, with large areas of medical need unexplored, have become serious in the last two decades. It has led to a diminishing focus on more intractable disease states, such as neuropathologies, which lack good biomarkers.

Risk Aversion

The commercial success of the multiple drugs focused on validated targets encouraged many stakeholders, including investors, to believe that such success was the norm. Though industry did try to identify novel targets, increasingly through genomics, they proved to be even higher risk, partly because they were not fully validated. Thus, when faced with a choice of predictable returns from successful validated targets or exploration of new ones, industry prioritised the former and was rewarded by investors for doing so. The result was a consolidation of effort on those self-same targets and a reduction in the breadth of the portfolio.

Consolidation

The wave of mergers and acquisitions from the 1980s onwards also contributed to a reduction in R&D productivity as the act of consolidation, rather than enhancing productivity, proved to be an organisational disruption which reduced the pipeline, created distractions and fostered an organisational structure at cross-purposes with product-driven value creation.

Regulatory Requirements

The final cause of productivity decline was found to be the growing requirements of regulators who have raised the standards of safety and efficacy, particularly for primary care, obliging companies to gather much more clinical data from many more patients. The increased costs of late stage clinical trials, together with higher hurdles for success, have required companies to make tougher choices about which projects have the best chance of success for a given R&D spend.

The ecosystem of innovation includes Big Pharma, biotech and academia. Identifying the most efficient and productive role for each of these multiple creative players is leading to calls for significant rationalisation. Perhaps the most critical decision facing the industry today is the extent to which excess capacity in the R&D function can be reduced without a resultant loss of core industry competency and further damage to R&D productivity. Different companies have signalled radically different approaches to this. At one extreme has been the defence of a broad portfolio and an accompanying warning to investors to lower their profit expectations. At the other has been a radical reduction in R&D expenditure. Investors still appear to lack conviction that the current R&D strategies of the industry can provide a sustainable and increasing return, though there are early signs of increasing confidence.

The Reimbursement Challenge

R&D productivity is intimately linked with corresponding willingness and ability of the payer to pay. The 1980s and 1990s marked a “Golden Age of Pharmaceuticals” during which the payer seemed to have a limitless appetite for new drugs. Although the race was for first and best in class, second, third and fourth could find a market too. The doctor decision-makers were persuaded of the value of the new generations of medicines, compared to the old and accepted product to product differences.

As a consequence their prescribing practices expanded utilisation and the range of products used. While doctors seemed unconcerned about the price implications, the payers were too dispersed to do anything other than passively endorse higher prices for the new medicines and the annual price increases (in the US) thereafter. Where the US led, Europe followed, and there too the industry proved able to increase sales volumes without too much pushback on pricing.

During this era of first and best in class, regulatory hurdles were

relatively low and pipeline pruning took place only if the drug was particularly unsafe or ineffective. The market signalled its willingness to pay for multiple products in key therapeutic areas and so industry responded to these large markets with clear targets by focusing its attention on them in a logical deployment of capital.

The expansion could not last. The increasing cost burdens of rising prices and expanding volumes (associated with life-long chronic disease therapies) led first to modest and then to more intense pushback. Trust began to erode as the price of incremental innovation in the new “me-too” therapies came to be perceived as over-reach for the limited added value they offered.

Payer pushback was first felt in Europe where there were a range of attempts to hold down escalating pharmaceutical budgets, including the introduction of black lists, negative lists, price cuts and jumbo groups (groups of drugs in the same therapeutic class, reimbursed at the

same level irrespective of differences in clinical effect).

At the same time, the new discipline of pharmacoeconomics began gaining ground and the language of doubt began creeping into the vocabulary in payer efforts to make qualitative assessment, to define value for money and to establish evidence-based protocols.

More recently, there has been a big increase in the generation of head to head comparative data on different therapies and more and more payers have begun to insist on generic substitution. Over time, decision-making has gradually passed from the physician to the payer – a shift that has taken place in both Europe and the US, despite the highly politicised nature of the debate about choice in the US market. In the process, the demand for evidence has become institutionalised to varying degrees and in different forms, across the range of payers globally, and is increasingly a condition of reimbursement.

Rethinking the Model

The result has been to find ourselves at a crossroad in which the relationships between the industry and its stakeholders have fundamentally changed. In the previous model, corporate and venture investors confidently allocated capital to R&D on the understanding that the industry’s judgement about what would succeed in the market was sound. The appetite of the payers for the products coming online ratified these assumptions. In the new model, in which payers are demanding evidence of value, particularly of incremental innovation and increasingly linked to price, sources of capital have become

increasingly risk averse, no longer confident of industry’s ability to predict what payers will be prepared to pay for.

Despite first appearances, this impasse presents the most significant opportunity facing the industry today as it dawns on the many players who will influence what happens next, the degree to which they share a common interest in finding solutions. The growth in patient groups, newly empowered by online information; the rise of the consolidated payer; the increase in the quantity and quality of real data about the comparative effectiveness of medicines, as well as efficacy and

safety; and the fact that the industry is already being heavily discounted by the financial markets provide not a threat, but an unprecedented opportunity to collaborate with other actors in the marketplace to identify the medicines society needs, and is able and willing to pay for. The definition of innovation, having passed from industry to payers, could become much more aligned with what payers want, what prescribers want and what industry scientists want: to make a difference with a new medicine. This could evolve into a “Shared Value” model in which the social contract is renewed to the mutual benefit of industry and society.

Recommendations

Determined to contribute to a “Shared Value” model the *PharmaFutures Working Group* identified the following responses from society, industry management and investors that it considers most likely to result in mutually beneficial outcomes. These would ensure that the industry is rewarded commensurately for meeting unmet patient need while providing appropriate returns for investors and recognising the constraints on society’s ability to pay.

Role of Societal Stakeholders

- Signal priority unmet needs and priority focus for treatments
- Coordinate work of Agencies dealing with the Pharmaceutical Industry
- Be prepared to collaborate with Industry

Government Agencies

- 1. Articulate a clear healthcare strategy** that gives a well-defined picture of what you see as the appropriate balance of health interventions, including prevention, treatment and cure across and outside the health system.
- 2. Encourage debates about future health policy** which incorporate discussions about efficiency savings involved in preventative and early interventions.
- 3. Clearly signal areas of unmet need in timely fashion to Industry** to enhance the industry’s ability to make appropriate investment decisions. Recognise that decisions about today’s application also serve as guidance for products just entering early development. In the absence of direct guidance about those early candidates, the signals are easily misunderstood.
- 4. Enhance multilateral collaboration** in signalling unmet need, e.g. at European level.
- 5. Expand collaborations** with industry on non-commercial unmet need which will require risk-sharing between government and industry; identify milestones for collaboration; collaborate earlier

in the development process, especially with R&D departments.

- 6. Coordinate health, regulatory and reimbursement policies and practices** so that they combine appropriate rewards for innovation with the need for pricing discipline.

Regulators, HTAs and Payers (Public and Private)

- 1. Collaborate** to minimise unnecessary duplication.
- 2. Harmonise** assessment criteria and rationalise data requirements across regulatory and health technology assessment entities (HTAs) throughout the development process, including streamlining pathways to approval which minimise unnecessary differences in filing formats, deadlines and requirements and post-marketing surveillance.
- 3. Enhance channels for providing scientific advice**, particularly at the earliest stages when advice and guidance (even tentative and subject to revision) is most valuable, e.g. multi-country/single-stakeholder collaboration (HTAs, Payers and Regulators, plus individual company) multi-stakeholder/ multi-country collaboration (HTA, Payers, Regulators, plus multiple companies).

- 4. Expand and increase alternative approaches to approval and reimbursement** including early conditional approval for specific patient sub-populations; reimbursement with evidence over time, where evidence can be generated post-launch and post initial reimbursement; and support research of products into higher risk areas of unmet medical need through enhanced exclusivity periods and/or priority regulatory review.
- 5. HTAs: consider a common format** for any reimbursement criteria.
- 6. Regulators: acknowledge the cost–benefit equation** in risk assessment and that the expense of longer studies to identify smaller differences leads to more expenditure on post-marketing surveillance and reduced expenditure on innovation.
- 7. Regulators: engage** with industry to reconcile the balance between patient risk (side effects) and reward (clinical benefit) particularly in those cases where the commercial opportunity is not large enough to justify the additional development expense, despite a meaningful unmet medical need.

Role of Biopharmaceutical Industry Management

- Enhance the credibility of management
- Improve innovation in the Biopharmaceutical Industry
- Rebuild the social contract through collaboration on value and reimbursement

Enhance the Credibility of Management

- 1. Define the company's core competence.** Review, rethink and rearticulate what the company does well; and how the business model is designed to exploit that skill/competency.
- 2. Reconsider the business model.** Acknowledge that long-standing business models may not be suited to deliver innovation and growth. Begin to reframe the model through:
 - Experimentation that supports the removal of excess capacity without undermining core competencies
 - Expansion of new R&D collaborations
 - Expansion of the collaboration in the pre-competitive space to improve understanding of disease biology in areas of unmet medical need, up to, in some cases, proof of concept in humans.
- 3. Be explicit about the capital allocation philosophy.** Identify where the company wants to invest, how it makes those decisions, define the required returns, outline the company's track record and the future milestones, specify how shareholders should factor these considerations into their decision-making.
- 4. Be significantly more consistent and transparent in communications.** Identify your strategy, communicate its evolution, be clear about the rationale for any changes, and communicate your core

competencies. Allow regular access to management beyond the C-Suite to enhance investor confidence in process and capabilities.

5. Be bold. Consumer perceptions and capital market valuations of the industry are at all-time lows so the risks of bold action are low. Don't be afraid to break from the pack, be proactive not reactive. For example, consider new product and service offerings, combined with medtech delivery systems; offer lower margin products in higher volume markets; build ties with truly independent patient groups and philanthropic entities.

6. Aggressively manage internal assets to create value. Be prepared to make necessary efficiency cuts, monetise non-productive assets, increase transparency. Explore new risk-sharing models.

Improve Innovation in the Biopharmaceutical Industry

- 1. Identify a clear R&D investment process.** Articulate it internally and externally, particularly to investors who will use it to judge future value. Once in place use it and don't ignore it.
- 2. Retool R&D to increase externalisation, increase experimentation and expand R&D collaborations.** This should include partnerships between companies, licensing, pre-competitive partnerships and, where possible, a general expansion of the pre-competitive space. Consider increased patent pooling, including areas of increasing commercial potential.

3. Streamline internal R&D to attract and retain talent. Build on existing initiatives to create the right environment for scientists to flourish, prevent the flight of talent post-consolidation, give scientists more "bench time" and fewer meetings, and outsource fixed cost infrastructure.

Rebuild the Social Contract through Collaboration on Value and Reimbursement

- 1. Foster collaborations** designed to agree criteria on what constitutes value and price accordingly.
- 2. Continue to provide greater pipeline transparency** with the timely posting of trial results, including failures.
- 3. Build on existing collaborations on unmet medical need** such as those designed to develop products for diseases of the developing world and neglected diseases.
- 4. Undertake risk-sharing partnerships** including novel clinical trial approaches and risk-sharing reimbursement agreements based on agreed outcomes.
- 5. Undertake early engagement** with payers and regulators to streamline regulatory requirements, throughout the development process, including post-marketing surveillance while meeting safety, efficacy and cost-effectiveness concerns.
- 6. Engage with regulators and payers** to rationalise data requirements across regulatory and HTA entities.

Role of Investors in the Biopharmaceutical Sector

- Continue to play a critical role in funding new drug discovery
- Use activist tactics to support sustainable R&D models and help bring change in its absence
- Retain a focus on the long term to achieve sustainable returns

Venture Capital and Private Equity

1. Continue to play the critical role of funding new drug discovery

platform technologies and novel products, in categories with unmet need. These investments often in start-ups and “biotech” companies, consortiums and public private partnerships increasingly provide the leads which feed development for Big Pharma. Any slowing of investment at this stage will directly reduce the eventual pipeline at those larger companies.

2. Be prepared to support new exploratory models of risk-sharing both within and outside established biopharmaceutical companies, to break the pattern of poor historic returns.

Specialist Healthcare Investors (long only and hedge funds)

1. Proactively articulate a strategic viewpoint to companies.

2. Where necessary, use activist tactics to help bring change to companies without a sustainable R&D model.

3. Evaluate companies on the basis of overall portfolio to allow for different volume/price trade-offs in different therapeutic areas to address unmet medical need.

4. Give clear signals to companies. Make sure companies executing well know that they have the support of their shareholders.

Generalist Investors

1. Retain the focus on the return on R&D investment and the ability to achieve a sustainable return above the company’s weighted average cost of capital. This will allow long-term, self-funded re-investment into R&D on an ongoing basis.

Appendix

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