Introduction

Changes and practical challenges to market access planning
In the past the pharmaceutical industry relied on old conventional ways of building influence with KOLs, believing the key to product success was merely conveying effective messages through efficient communication with physicians who prescribed the drugs. Currently a need for new conventional wisdom has arisen due to the increasing types of hurdles for market access. When confronted with a complex environment in which multiple stakeholders come with multiple requirements, in addition to multiple (and costly) HTA. The key to product success is effective management of payers\(^1\). Payers are healthcare budget holders, including insurers, pharmacy benefits managers and government agencies. As a result of this balance shift, in which payers become more powerful, the impact of physician detailing on launch outcome drops. Since payers are increasingly the most influential stakeholder, they must be approached as customers. Ensuring that payer needs are fully understood recognized and met during product development. This requires meeting payers’ evidence requirements while effectively communicating value propositions. This ‘payer marketing’ can be efficient only after attaining all the necessary skills and knowledge related to payer marketing, including applying creativity, qualitative and quantitative research and efficient on going communication.

Pharmaceutical companies are driven to find many new and innovative approaches in order to secure market access for new pharmaceuticals. A challenge to market access may include expensive medication for novel treatments which boost drug spending. To succeed meeting the challenge of creating innovative approaches pharmaceutical executives need first to revamp their methods for developing and marketing drugs. Market access planning should be an integral part of their organization, while balancing clinical and economic value in product development and commercialization decisions\(^2\).

New set of assessments for successful ‘payer marketing’
The measures of market access have changes accordingly. In the past national/government bodies had the role of negotiating price and/or reimbursement namely internal or external referencing. While currently local and regional bodies have the responsibility to determine how to spend healthcare funds through HTA, guidelines and substitution While in the future we can foresee a need for proactive investment into health care areas of focus or relevance through commissioning and payer funded trials\(^1\).

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1 Janice Haigh Market Access – practical challenges for the pharmaceutical industry 2010 Astellas Pharma Europe

2 Cameron McClean and Thomas Croisier (2010) Big Pharma’s Market Access Mission
To ensure meeting goals of ‘payer marketing’ requires a number of novel approaches: determining investment in payer research vs. physician research; researching payer needs and views in addition to their attitude to price; using payer research to inform the TPP or trial design; determining the process for defining unmet needs; shaping new measures for R&D performance and finally testing value messages with payers before submitting a dossier.

To overcome inadequate launching of new medications, new arrangements need to be made between customers and pharmaceutical manufacturers. These arrangements will on the one hand secure market access on the other hand they are conditioned to have a reduced risk to the payers. Executives at pharmaceutical companies can no longer rely on the existing set of brand strategies for market access. Instead the need to integrate the payer perspective throughout the full set of decisions they make.

**Hurdles to market access**

Gaining market access for new pharmaceuticals can be successful with the awareness to various hurdles. In the past, overcoming the 3 hurdles to Obtain Regulatory Approval entailed proving Efficacy, Safety and Quality of a product at launch. This was sufficient to gain market access and patient access to new drugs and new biopharmaceuticals. The changing pricing and reimbursement environment requires focusing on the time lag between applications for approval and granting of marketing authorization. The fourth and fifth hurdles pertain to reimbursement and pricing of approved drugs. Within the last decade government agencies have started sharing best practice of technology assessments (health economics) around the world, comparing pricing and reimbursement mechanisms in an attempt to find a local solution.

Achieving market access was, in nationally regulated reimbursement countries, essentially a presentation of clinical benefits and a “negotiation.” Clinical benefits were driving the process; bringing to market drugs with unmet clinical needs has been the driving force behind “state” reviews. Stimulating innovation, R&D and local investments by the pharmaceutical industry have been key elements in these negotiations. In the last 15 years, increasing data and evidence is demanded from the pharmaceutical industry when they launch new products. Risk benefits requirements have increased (safety focus). Risk management programs are now required for all New Chemical Entities;

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effectiveness versus established gold standard is required rather than just placebo controlled⁵.

The fifth hurdle to marketing access is pricing. Proving “value” for money has increased this ‘Pharmaco-economics’: cost effectiveness and cost utility. Economic evaluation has become part of the equation in pricing and reimbursement decisions. Measuring “Value” is challenging since it’s not an exact science. This is what Pharmacoeconomics studies aim to deliver, an unmet clinical need. By showing that the clinical and economic burden of the disease is not addressed by current treatment rather could be fulfilled by a new product so its “value” can be quantified. Impact on clinical management has impact on drug budget as well⁵.

Showing patient-relevant outcomes with a new treatment can show “value” in adopting a new treatment. Showing the adoption of a newer more expensive drug can impact direct or indirect costs of managing a patient, is another way of showing value. As payers seek to reduce uncertainty for paying for drugs for which evidence of clinical and/or economic benefits is insufficiently robust at launch, new arrangements are being made between payers and manufacturers to enable market access under conditions that limit the risk to payers³.

As the measurement of “value” is subjective, a new drug value and its adoption can vary enormously. Variation of Perceived and Quantified “value”: Same compound, with the same development program, with the same promotion strategy and expenses and the same “global commercial strategy” can lead to various adoption rate and speed in different countries. Thus delays and perceived “value” are measured and perceived differently⁵.

**The future of value-based pricing** To elaborate and clarify the notion of price as a function of value there are 4 basic situations:

- When prices are high and perceived incremental value to patient is strong will result in broad market access with wide adoption. With the same result when prices are low with a limited perceived incremental value to patient, although wide adoption will happen if there’s a lack of alternates.
- When prices are high with a limited perceived incremental value to patient will result in payer restrictions, while providers will relegate to late lines of therapy.
- And finally when prices are low and perceived incremental value to patient is strong will result in foregone profits to pharmaceutical manufacturers.

This favorable pricing environment will continue through 2010, while conditions facilitating higher prices will erode beyond 2010. Since patient cost sharing increases price elasticity of demand. Direct government involvement, first through federal programs, is increasingly likely 2014 onward. Generics and biomarkers mitigate pricing pressure. Generics provide “head room” for

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innovative and new products. Biomarkers improve payers/employers’ perceived value. The key is innovation, matched to outcomes⁶.

**Pharmaceutical policies** pharmaceutical manufacturers when debating which marketing access scheme to go with must take into consideration a number of factors, starting with pharmaceutical policies, which have a direct affect on drug use, healthcare utilization, health outcomes and expenditures. These pharmaceutical policies are laws, or financial orders which are made not only by governments rather also by non-government organizations or private insurers.

As already stated one of the major challenges to many health systems is the growing expenditures on prescription drugs. Pharmaceutical policies are different according to the country, in the US direct patient drug payment policies include:

- Caps meaning the maximum number of prescription drugs reimbursed
- Fixed co-payments meaning the patients pay a fixed cost for each prescription drug (direct cost-share).
- Coinsurance meaning patients pay a percentage of the price of prescription drugs reimbursed.
- Ceilings meaning patients pay the full price (or up to a ceiling cost, then availability is reduced or free).
- Tier co-payments meaning co-payments assigned accordingly, generic or brand drugs.

The original intention in caps and co-payment policies are to be an incentive to discourage unnecessary or subsidiary utilization, and furthermore to reduce the financial burden on third-party payers by shifting parts of the expenditure from the insurer to the patients, consequently increasing their financial responsibility for prescription drugs.

Consequently a recent Cochrane review indeed concluded introducing or increasing direct co-payments reduced drug use and saved plan drug expenditures. Accordingly patients chose the option of drug discontinuation or cost-sharing. Furthermore they found this policy brought forth reductions for life-sustaining drugs or drugs crucial for treating chronic conditions as well as other drugs⁷.

In order to address the hurdles to market access, innovative strategies are being employed by payers and manufacturers alike. These approaches and strategies

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have been employed in international markets including the US and Japan as well as the main European markets: France, Germany, Italy, Spain and the UK. The development of innovative approaches to market access, requires first an examination of the existing market access schemes in key pharmaceutical markets, including awareness to the pros and cons of these different types of market access schemes.

**Market access schemes**
Gaining market access for new products during the pricing and reimbursement process has become more challenging for pharmaceutical companies. Initiatives are under way to improve market access of innovative products, including patient, value-based pricing and pre-licensing access schemes; risk-sharing agreements and pay-for-performance schemes (or rebates for non-responders).

Generally speaking, innovative market access schemes, which recognize the value of patient access, are classified in two types: finance-based in which discounts and rebates are linked to usage at patient or population level; or performance-based/outcomes-based in which reimbursement is linked to performance guarantees or the generation of further clinical evidence.

While some overlap between the two may exist. For example, finance-based schemes that link rebates or discounts to the response of patients treated with the drug comprise an outcomes element. Finance-based schemes are preferred by payers since they are simple to administer and do not involve patient monitoring.

Market access schemes place the emphasis on offering patients access to needed medications. One aim of patient access schemes is to give earlier access to innovative drugs for small patient populations. Typically in patient access schemes drugs are provided free for a period of time. Taking into consideration the factor some pharmaceutical manufacturers are building into their patient access schemes, in order to minimize the burden on the payers. Pre-licensing access schemes offer earlier access to medicines that have yet to receive official approval.

**Outcomes-based schemes** These performance-based contracts can link pricing and reimbursement to a predetermined specific endpoint or to a defined patient response. These 'coverage with evidence development' schemes as well or payment by result schemes are based on outcomes achieved in practice. These schemes enable patient access to novel treatments for diseases with unknown long-term outcomes and/or cost-effectiveness. These efficiency stipulation schemes or effectiveness guarantee schemes offer a way of enabling the pharmaceutical manufacturer to gain market access earlier without compromising the launch price and reducing the uncertainty of product performance. However they are regarded as complex, involving additional costs and resources.
Schemes involving rebates, discounts or free supplies maintain the pharmaceutical manufacturers' list prices\(^8\).

**Risk-sharing schemes** In Adamski et al (2010) review on risk-sharing schemes in Europe they explain the incentive for payers to adopt these risk-sharing schemes is a way to limit the growth in pharmaceutical expenditure while ensuring a maximum health gain within limited budgets. Furthermore limiting 'off label' prescribing or insuring prescribing only to identified sub-populations where the value of the technology is greatest. The new definition they propose relates to the fact that in practice, the risk-sharing agreement depends on the setting and scope while realizing the mutual obligations of both payers and pharmaceutical companies. This depends on the condition defined as a "risk". This "risk" can result in pharmaceutical expenditure higher than agreed thresholds or a lower health gain from a new product which reduces its value. One result of this new definition is that a large number of 'risk sharing' schemes with pharmaceuticals incorporate not only performance-based/outcomes-based models, rather also financial-based models. These include price-volume agreements/budget impact schemes which focus on controlling financial expenditure with pharmaceutical companies refunding over budget situations as well as. Or patient access schemes which include price-capping schemes, which focus on controlling the financial impact but from an individual patient perspective\(^9\).

There are many and various schemes that have been developed and implemented in different countries with various financial outcomes for the pharmaceutical companies: US. with patient access schemes and Canada with price-volume agreements; the UK and Italy are leading the way in Europe with the development of risk sharing schemes.

**US**
Patient access schemes were adopted by Genentech, to help address public concern over the rising prices for cancer drugs. In 2006 patient access schemes was used to cap the total cost of Bevacizumab at $55,000 per year for patients below an income of $75,000 per year. Costs are a particular issue especially for patients with breast cancer, as well as earlier stages of lung and colon cancer, with the scheme resulting in a 50% reduction or more in costs for one year of treatment. ImClone Systems and Bristol-Myers Squibb also adopted patient access schemes. In 2006 they announced lower-income patients who reached a price

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cap of approximately US$10,000 monthly for Cetuximab, would be supplied at a large discount with extra medicine or even for free. Amgen in 2006 introduced an oncology patients scheme to provide financial assistance for patients prescribed Panitumimab for the treatment of metastatic colorectal cancer when co-payments reached 5% of patient's adjusted gross income\(^9\).

**Italy**

Risk-sharing agreements enable early schemes as early access to new expensive drugs, mainly oncology products. Risk-sharing agreements have become the norm for gaining market access for cancer drugs in Italy. For example Bevacizumab for the management of approved cancers cannot exceed €25,941 per year\(^8\). Earlier access to expensive and innovative drugs in Italy is facilitated through the growing use of risk-share agreements. Italy pioneered one of the earliest risk-sharing schemes in 2000 when the government launched the Cronos project to assess the possible reimbursement of Alzheimer drugs. The Italian authorities have engaged in a risk-sharing scheme thus providing patient access to new drugs in a managed system. Rebates for non-responders as the case of Aclasta in Italy (and Germany) is a variation on the pay-for-performance scheme\(^8\).

**UK**

A key issue in gaining UK market access is through cost-effectiveness schemes. Other initiatives including patient access schemes, value-based pricing and pre-licensing access which are all focused on improving access to innovative products. Taking into consideration the environment for pricing and pre-licensing and market access in major markets is undergoing change. One of the earliest schemes was risk-sharing agreements in the UK. This scheme enabled early access to new expensive drugs for multiple sclerosis treatment, leading the way for future outcomes-based schemes. Pay-for-performance schemes are in place in the UK (for example for Velcade) where payment is received only in the case of patients with a positive response to the medication\(^7\).

NICE (National Institute for Health and Clinical Excellence) in the UK has adopted patient access schemes to increase the value of new medicines. One example includes cetuximab for the treatment of metastatic colorectal cancer. According to this patient access scheme Cetuximab will be rebated as free stock (1 vial per 8 utilized) when used in combination with Folfox. Another example includes Sunitinib for patients with metastatic renal cell carcinoma. In which the first treatment cycle (6-weeks costing an average of GB£3139/patient) is provided free via through the patient access scheme. Subsequent cycles are funded by the NHS until disease progression. The Department of Health considered the scheme did not constitute an excessive administration burden on the NHS\(^9\).
**France**
Finance-based schemes for example price-volume agreements are the norm in France. Price-volume agreements cap costs per patient, dose or overall expenditure. France uses payback schemes for excessive sales by therapeutic class, based on the pharmaceutical company’s agreed turnover with annual financial adjustments. These change yearly and include regular price reviews, based on the average daily costs/dose at time of reimbursement. Adoption of these payback schemes in 2008 involved Naglazyme® for the treatment for mucopolysaccharide type VI disease, and Soliris® for the treatment of paroxysmal nocturnal haemoglobinuria. Price-volume agreements are common in Canada and Australia as well. The rate of development of price-volume agreements in France is comparable to the situation in Australia where some 80 price-volume agreements have been developed with the Pharmaceutical Benefits Advisory Committee (PBAC). While in Canada, price-volume agreements are almost mandatory in the major provinces.

**Germany**
Examples of price volume agreements in Germany are the rebate contracts existing between the Sickness Funds and pharmaceutical companies to accelerate access and/or boost market access of certain drugs where there are concerns with their value. Current schemes include the insulin analogues, olanzapine, risperidone, clopidogrel, zolendronate (Aclasta®), mycophenolic acid (Myfortic®), everolimus (Certican®), and cyclosporine (Sandimmun®).

**Hungary**
The price volume agreement in Hungary includes a general payback scheme which has been in operation since 2003 based on individual products as well as total pharmaceutical expenditure. Introduction of the law regulation in 2007 concerned with the pricing criteria for pharmaceuticals has only limited exceptions. Under this scheme, pharmaceutical companies are obligated to pay the Ministry 12% of their total reimbursed sales each year. In addition, the first 9% of any budget overspend for a given class; the cost is shared by the social health insurance and pharmaceutical companies (who pay a greater percentage). When overspend exceeds 9% of the agreed budget, all the additional costs are covered by the pharmaceutical companies. The payback in 2006 was 22.5 billion HUF (€90 mn - 5.69% of the budget).

**Japan**
The strict regulatory requirements and the time it takes getting new drugs registered in Japan often causes a serious delay in access to the Japanese market. This situation causes delaying Japanese market access by up to five years after a drug's initial market launch in the US or the EU.
It is our understanding that Pharma Company would like to establish a framework for innovative market access schemes. To reach this aim Pharma Company would like to develop in this framework a solid knowledge base about innovative access schemes. In addition to providing the knowledge base of worldwide used market access schemes, Proposal company would also provide information that would expand and further populate this framework. As we understand Pharma company would like to use this framework developed by Proposal Company to educate members of the Global Market Access (GMax) group and the broader Pharma company organization on various innovative elements and approaches to market access. As a final result of this project, Pharma Company would like to substantially improve their understanding of the worldwide market landscape position and adoption of market access schemes to further populate a database of target countries for successful market access.

Proposal company would deliver a framework for market access that highlights target countries and regions. The framework will include past innovative schemes used to successfully gain market access.

Proposal company also understands that Pharma company is seeking an estimation of market size for each identified access scheme. We will provide a data driven estimate of the market potential for specific access schemes. This will be in addition to the information provided by the market access framework.

Proposal Company would deliver additional information for the market access framework that highlights future benchmarks of the market place to market access in the target countries and regions.

It is also a goal of this study to provide a preliminary reimbursement perspective in consideration of future benchmarks of the market place. We would like to identify any regulatory practices or other reimbursement factors that may cause hurdles or challenges.

Proposal Company will primarily focus on defining critical areas of market access innovations. These include as first priority strategies as: risk sharing schemes, performance-based/outcomes-based schemes, finance-based schemes, differential pricing and performance guarantees.

Proposal Company will also seek information regarding innovative market access schemes that are used on market place or near-market place usage that could provide immediate impact in a 3 year or less timeframe.

As a secondary focus, we will include strategic pharmacy management outcome guarantees for launch compounds portfolio setting deals will also be explored.
This study will focus on the following geographic regions:

- **North America**
- **Western Europe**
- **Eastern Europe**
- **Japan**

In addition, Proposal company will also seek any information necessary to complete the project from other developed global accessed markets.

**OBJECTIVES**

- Survey the worldwide marketplace for innovative market access schemes, with the goal of creating a market access framework of existing and emerging market access schemes
- Suggest organic and inorganic strategies for growing business
- Improve understanding of market landscape position for internal product development and possible business development and licensing activity affecting market access
- Validate findings of Pharma Company's previously conducted internal exercise

**RESEARCH OBJECTIVES**

The primary objective of this research project is to identify emerging market access schemes and further source and validate those opportunities. Furthermore, we will source on-market or near market innovative market access schemes which may fit Pharma company's strategic goals.

Proposal Company will rely on its Proprietary Database of over 3,000,000 life science opportunities to uncover and identify the most viable target market access schemes and strategies. The database is highly granular with a strong representation of aligned segments with a particular emphasis on hard to identify transactional opportunities which have been sourced through primary research with technology transfer centers, BD&L executives and R&D directors.
By coupling our internal database with our Primary Key Innovation Leader Research, we can source market access schemes and strategies which may fall "under the radar screen" of many BD&L efforts.

**PRIMARY RESEARCH (KEY INNOVATION LEADERS)**

A Key Innovation Leader questionnaire will be developed through a collaborative effort with Pharma Company Pharmaceuticals in order to ensure that the focus of this project is being addressed. The questionnaire is to be used as a platform for exploration and discussion. All interviews will be conducted directly by Proposal company Principals and Research Team who have the autonomy to probe deeper and maneuver through unique issues that arise during discussion with the KILs – what we refer to as improvisational interviewing. Our Research Team is able to select the most appropriate questions to ask each KIL due to our extensive knowledge and involvement with the project’s goals. These interviews are conducted individually, which allows us to focus directly on the expertise that each KIL possesses. Improvisational interviewing yields valuable qualitative interview data unlike structured interview surveys. Instead of merely moving from question to question, our Research Team is able to adapt based on KILs’ response to questions, thus obtaining additional insight.

To complement our Primary Qualitative Key Innovation Leader research we will concurrently perform secondary research from syndicated, internal, and public sources. We believe secondary research will provide us with useful data regarding the challenges and direction of market access schemes and strategies.

Our Secondary Research Methodology and its role in the project’s outcome are discussed in further detail below.

Proposal company believes that through the effective coupling of primary KIL insight and secondary research – along with our
partnership with Pharma Company we can obtain exceptional insight into innovational market access.

Our research module begins by concurrently identifying and recruiting a customized panel of Key Innovation Leaders (Table 2) and developing a project specific Key Innovation Leader study guide/questionnaire.

Table 1: Examples of Potential Key Innovation Leaders

Table 2: Examples of Potential Key Innovation Leaders

Proposal Company proposes to concurrently supplement our primary research with secondary research and trendspotting analysis. By combining primary and secondary research, we are able to gain insight into practitioner attitudes and financial possibilities – including preliminary reimbursement perspectives. Secondary research used to supplement our primary research and trendspotting includes:

**Syndicated**
Proposal company has established relationships with a variety of syndicated information providers within the pharmaceutical market and we currently subscribe to over 60 (sixty) subscription databases.

**Publicly Available**
Proposal company conducts significant market research within the public domain. We have expertise in identifying key market data through journal and trade publications, online subscription databases, market research data hubs, proprietary data sources and archival research.

**Internal**
One of Proposal company key assets is the market research previously conducted that resides “in-house”. Our ability to leverage this data significantly reduces the time constraints associated with providing the required deliverables.
TREND SPOTTING

Identifying market demand and receptivity; unmet needs; and trending analysis requires primary and secondary research to uncover emerging patterns and business opportunities for innovative market access.

We do not guess trends; we detect, analyze and evaluate them to make evidentially supported projections. For this project, our challenge is to evaluate the new opportunities for targeted successful market access. Harrison Hayes’ proprietary panel of KIL’s has significant insight into the market segment, the direction the industry is going and challenges pharmaceutical companies will face. They are on the cutting edge of trends and function as a valuable resource for understanding the future of successful market access.

Examples of trends that we will uncover include:

- Assess the market potential for future successful market access schemes within each region with a focus on geographical nuances (Ethnographic and Netnographic Analysis)
- Changing trends in adoption of market access schemes.
- Unmet payer needs in the applied market access scheme in each region discussed
- Cutting edge approaches and new innovations of market access schemes
- Future potential innovations for market access
- Material science innovations which may impact change in new product development, reimbursement and pricing

Trending research is an integral part of a successful research initiative, and Proposal company is confident our trendspotting methods will provide Pharma company the necessary insight into innovative market access schemes.
The Final Deliverable will include the following:

- A market access framework of existing and emerging innovative market access schemes and strategies, in the worldwide marketplace. Highlighting target countries and regions. The framework will include past innovative schemes used to successfully gain market access. Proposal company has already performed an internal exercise to populate this database. The framework will serve to 1) validate the current findings and 2) further expand/populate the database of market access innovations. An estimate of market size for each identified access scheme. -A data driven estimate of the market potential for specific access schemes. This framework will aid in highlighting specific areas of interest that address the same (or similar) markets, and further insights on the potential size of each market.
- A framework of innovative market access schemes that highlights future benchmarks of the market place for successful market access in the target countries and regions.
- A preliminary reimbursement perspective – as reimbursement and pricing are key criterions in consideration of future opportunities. Preliminary direction while identifying any regulatory or reimbursement or pricing factors causing potential hurdles or challenges.
- Defining critical areas of market access innovations including: risk sharing schemes, performance-based/outcomes-based schemes, finance-based schemes, differential pricing and performance guarantees.
- Information regarding innovative market access schemes that are used in market place or near-market place providing immediate impact in a 3 year or less timeframe.
- Information regarding strategic pharmacy management outcome guarantees for launch compounds portfolio setting deals.