Commercial process for pharmaceutical drugs

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Introduction

Pharmaceutical companies need to achieve the regulatory approval of their pharmaceutical products, in order to market the product for treatment of a disease. In addition, they also need to negotiate the price of the products with the relevant public authorities, in order to secure public reimbursement of the patient expenses for using the product. The company pricing of a pharmaceutical product is dependent on the reimbursement status. This reimbursement negotiation is becoming an increasingly important bottleneck for the companies because of the growing need for public authorities to cost control their health care budgets.

The market of prescription medicine is thus very different from most other industrial markets as outlined in the figure and table below.

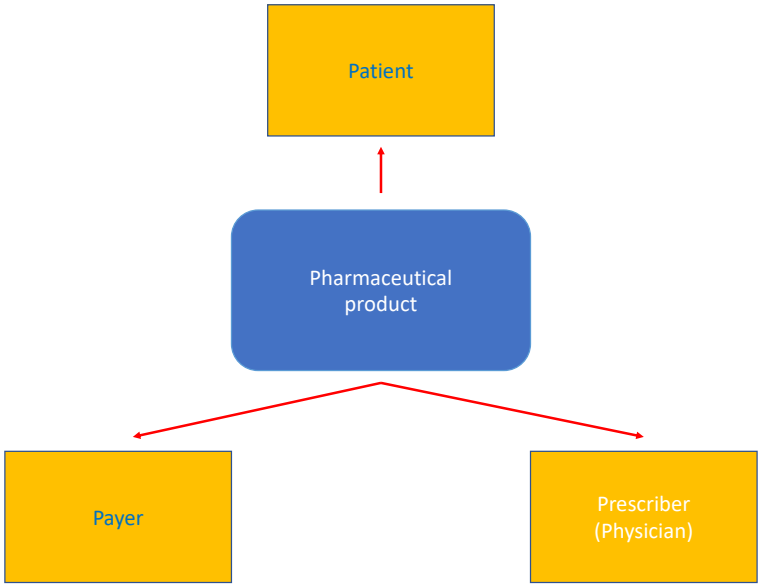

Figure. Pharmaceutical products have at least three customers.

	Chooses the medicine for consumers	Pays for the medicine	Consumes the medicine
Normal market	Consumer	Consumer	Consumer
Prescription medicine	Prescriber	Government/ insurer	Patient

Table. The prescription pharmaceutical drug market is different from other markets.

The pharma companies and the payers of the medicine have clashing objectives. The pharma company objectives are to the widest possible range of disease indications for the medicine (Big market volume), full reimbursement and highest possible price. The payer objectives are to avoid premium on price and a limited reimbursement payable only in those disease indications, where the medicine is most effective. The importance of reimbursement means, that the purchasing power is shifting from individual physicians to integrated health systems. Patients are becoming more knowledgeable active healthcare consumers.

In order for the pharmaceutical products to receive regulatory approval, earn reimbursement and stand up to competing products, they need to have superior properties compared to competing products in relation to their efficacy, safety and/or convenience for patients as specified in their product profile.

The product profile should address unmet medical needs of the patients. Unmet medical needs' means a condition for which there exists no satisfactory method of diagnosis, prevention or treatment authorised in the community.

Drafting a buyer utility map may outline product or process features important for the patients. A value proposition is a description of the improvements a patient will realize in terms that are meaningful to the patient.

Examples of product profile parameters are listed below.

Citalopram

Efficacy	Safety	Patient convenience
Faster onset of action (days)	Lower concentration needed for efficacy	

Insulin

Efficacy	Safety	Patient convenience
Blood glucose lowering activity associated with fast acting analogs of insulin respectively long-acting analogs of insulin	Fewer hypoglycemic episodes	Better devices for injection

Monoclonal antibodies against TNF

Efficacy	Safety	Patient convenience
High proportion of patients benefitting from the treatment	No or few infections with the treatment	Fewer injections

Table. Examples of overall product profile parameters.

Below figure illustrate how different parts of a product profile may become important over time. The early production of animal derived insulin made it possible to treat patients with diabetes and thus efficacy was a priority. Animal insulin do however cause side effects as our immune system react against the foreign animal derived product. Recombinant DNA methods (and peptide chemistry) made it possible to mass produce human insulin, which are tolerated much better by our immune system. Scaling of the manufacturing process also made more cost-effective manufacturing processes possible. The human insulin products have in recent years been replaced by the insulin analogues, modified insulin molecules, with modified pharmacokinetic properties. The insulin analogues offer better convenience to the diabetes patients.

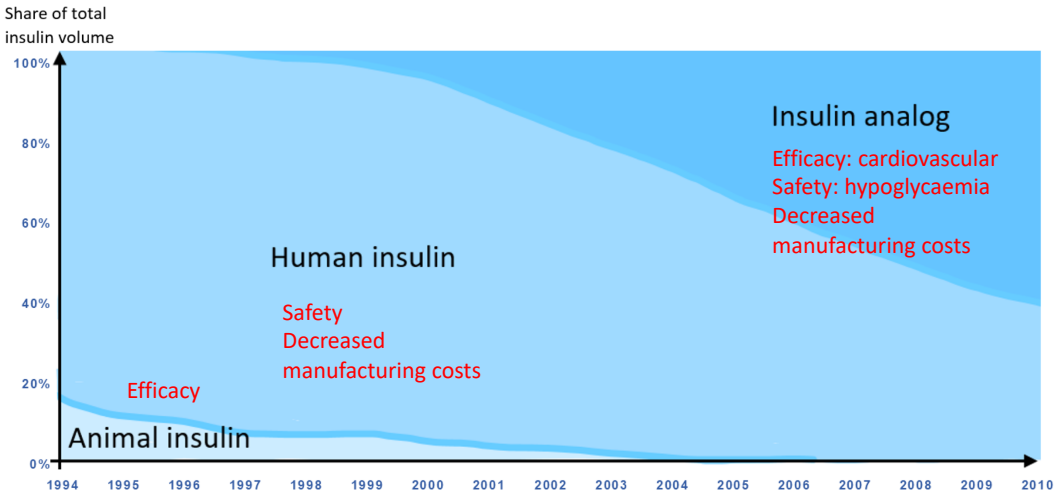

Figure. Changing nature of insulin products over time.

Value is an expression of the improvement(s) a new product or technology and its associated services offer relative to the incremental cost.

The assessment of value of a pharmaceutical product is evolving from being product specific to outcomes oriented.
Examples of value propositions include:

- *Reduced need for future treatment*
- *Improved compliance*
- *Ease of administration*
- *Reduced time of treatment*
- *Reduced cost of treatment.*

Differences in the approach to assessment of pharmaceutical drugs appear to have led to differences within different countries in their decisions about their reimbursements of different medicines for patients. Public authorities and insurance companies may thus analyse and conclude differently in relation to the use of surrogate endpoints, the importance of patient voice, comparator issues in clinical trials and dealing with uncertainty and available evidence (Shah K. et.al. 2013).

Drugs that are approved for treatment of patients undergo a lifecycle in their use in patients and in the sales, they generate. A product lifecycle may outline the course of a pharmaceutical product´s sales and profits over its lifetime. A traditional lifecycle of a small molecule drug is the initial introductory and growth phases, followed by the mature phase, which sees maximal use and sales of the

drug. Typically, due to patent expiry or introduction of new more effective treatments, the use and sales of the drug will decline in the expiry phase (see the Citalopram example later). The time to recover R&D´s cost´s for pharmaceutical products have been compressed in recent years.

There are different definitions of peak sales, such as the maximum sales the drug will reach in its life cycle as peak sales. The peak sales number is the net sales the company makes with the drug offering.

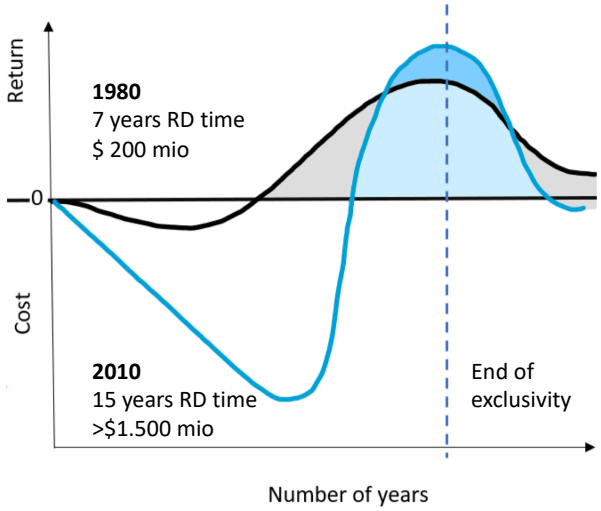

Figure. Product lifecycle for a small molecule drug.

A pharmaceutical market are the social interactions that allow buyers and seller to exchange information, products, services, and payments. Marketing is an organisational function and a set of processes for creating, communicating, and delivering value to customers and for managing customer relationships in ways that benefit the organisation and its stakeholders.
A market strategy is typically focusing on the four P´s, Product, Price, Promotion and Place.

Marketing and sales of pharmaceutical products are directed against the relevant disease indications and are typically focused on specific market segments. Segmentation may be based on patient symptoms and risk factors, the other treatments patients may receive, the exact health care provider for the patients, the relevant payer etc.

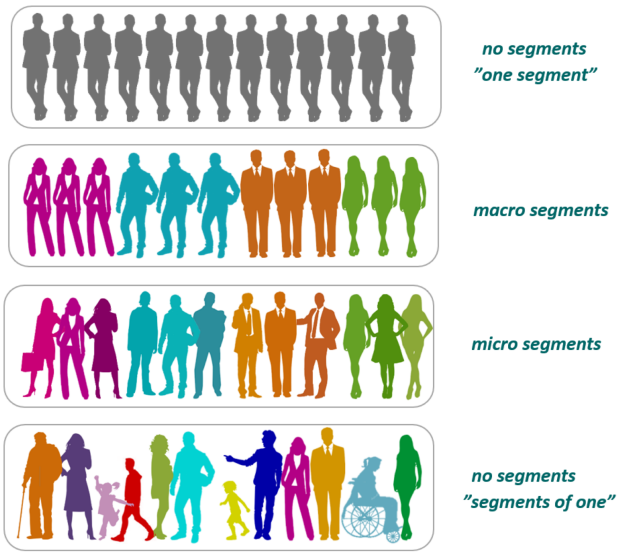

Figure. Illustration of different segmentation levels.

Each segment has certain characteristics such as number of patients within the segment and their geography, demographics, clinical risk factors, attitude towards health and health care providers, existing treatments, attitude towards new technology, self-pay vs. reimbursement.
Segmentation may as one example be analysed in a hospital or homecare market, which may be of a public funded or private funded nature.

The core requirements to segmentation

- **Segments must be stable** – if not, firms will find their customers in one segment one day and another one the other day.
- **Segments must be intuitively understandable for all employees** – if employees are not able to segment customers "on the spot", they are not able to service customers in the appropriate way, thus the segmentation is not executed.
- **Segments must be effective in the market** – if a segmentation does not mirror those differences which are important for customers, the segmentation cannot be used for differentiating customer strategy.

Targeting of customers deals with the selection of customers in the right market segment and is outlined in a market strategy.
Positioning refers to the sales strategy to these customers and relates to assets, such as first to market, strong distributor network, patents and brands.

Primary health care is an approach to health and wellbeing centred on the needs and circumstances of individuals, families and communities. Primary health care ensures people receive comprehensive care, ranging from promotion and prevention to treatment, rehabilitation and palliative care as close as feasible to people's everyday environment. The general practitioners, the family physician, the physiotherapist are the usual primary health care providers.

Secondary health care includes acute care: necessary treatment for a short period of time for a brief but serious illness, injury, or other health condition. This care may be found in a hospital emergency department but also outside the hospital setting. Secondary care also includes skilled attendance during childbirth, intensive care and medical imaging services.
Secondary health care providers include cardiologists, urologists, dermatologists and other such specialists. The health care services include acute care, short period stay in a hospital emergency department for brief but serious illness.

Tertiary health care is a specialised consultative health care for inpatients. The patients are admitted into these centres on a referral from primary or secondary health professionals. Tertiary health care is provided in a facility that have personnel and facilities for advanced medical investigation and treatment. Services provided include cancer management, neurosurgery, cardiac surgery and a host of complex medical and surgical interventions. Advanced diagnostic support services and specialised intensive care which cannot be provided by primary and secondary health centres are available at the tertiary health centres.

Diffusion of innovations is a theory that seeks to explain how, why, and at what rate new ideas and technology spread. The categories of adopters are innovators, early adopters, early majority, late majority, and laggards as outlined in the figure.

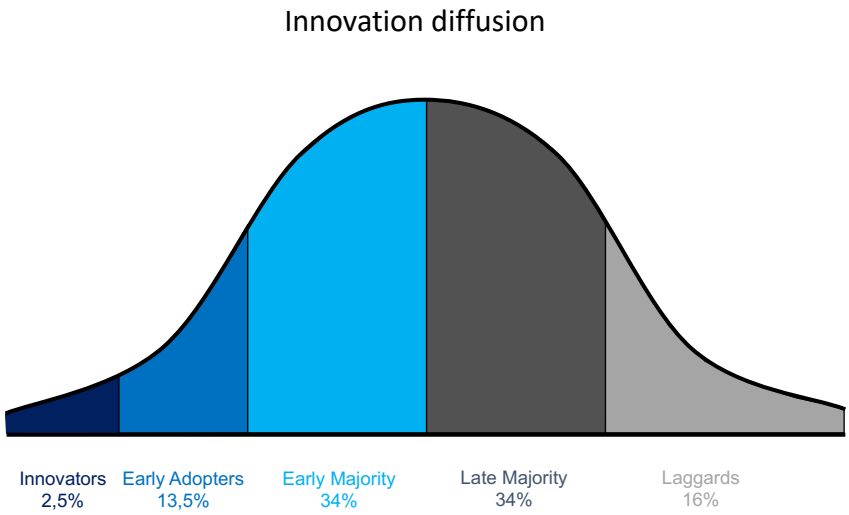

Figure. Diffusion of innovation into different customer groups.

The time period for innovation diffusion varies a lot depending on the type of product or service.

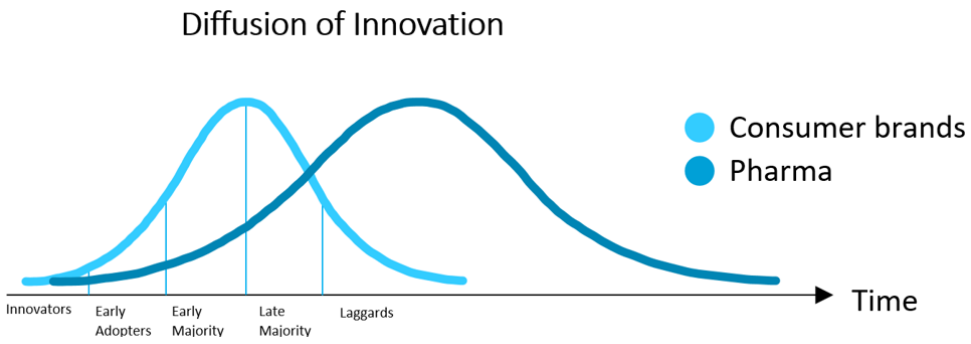

Figure. Different time periods for diffusion of innovation.

A portfolio diagram (BCG matrix) helps the company allocate resources and is used as an analytical tool in strategic management and portfolio analysis.

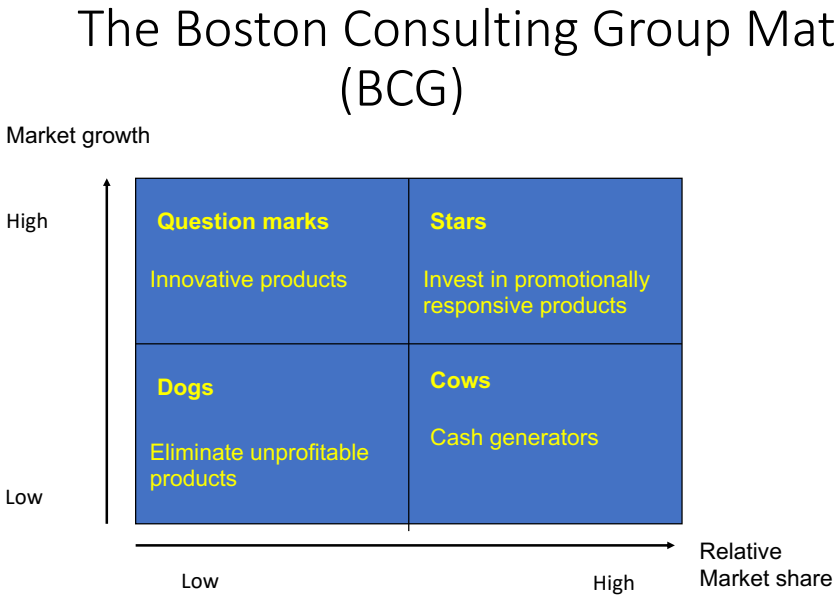

Figure. Outline of a portfolio diagram (BCG matrix).

To use the chart, analysts plot a scatter graph to rank the business units (or products) on the basis of their relative market shares and growth rates.

- ***Cash cows*** is where a company has high market share in a slow-growing industry. These units typically generate cash in excess of the amount of cash needed to maintain the business.
- ***Dogs***, more charitably called *pets*, are units with low market share in a mature, slow-growing industry. These units typically "break even", generating barely enough cash to maintain the business's market share. *Dogs* should be sold off in many cases.
- ***Question marks*** are businesses operating with a low market share in a high-growth market. They are a starting point for most businesses. Question marks have a potential to gain market share and become stars, and eventually cash cows when market growth slows. If question marks do not succeed in becoming a market leader, then after perhaps years of cash consumption, they will degenerate into dogs when market growth declines. Question marks must be analysed carefully in order to determine whether they are worth the investment required to grow market share.
- ***Stars*** are units with a high market share in a fast-growing industry. They are graduated *question marks* with a market- or niche-leading trajectory, for example: amongst market share front-runners in a high-growth sector, and/or having a monopolistic or increasingly dominant unique selling proposition.

The expected sales of a pharmaceutical drug depend on the disease indication and depend on the drug category, original versus copy product, and if a prescription is required or not (over the counter (OTC) drug). The world-wide pharmaceutical markets are outlined in the below tables.

	Swine Flu Contribution				1.0	7.9	5.4	1.5	1.6	1.6	1.6	1.7	1.7	1.7	1.7
WW Prescription Sales ($bn)															
Year	**2004**	**2005**	**2006**	**2007**	**2008**	**2009**	**2010**	**2011**	**2012**	**2013**	**2014**	**2015**	**2016**	**2017**	**2018**
Generics	27	32	40	46	53	52	59	65	70	74	78	83	88	92	96
Generics as % of Prescription Drugs	*5.9%*	*6.5%*	*7.4%*	*7.8%*	*8.2%*	*7.9%*	*8.8%*	*9.1%*	*9.8%*	*10.0%*	*10.3%*	*10.5%*	*10.6%*	*10.7%*	*10.9%*
Prescription Drugs excl. Generics	428	461	499	548	591	605	616	651	639	659	681	710	739	765	788
Growth per Year	*+11.0%*	*+7.8%*	*+8.2%*	*+9.8%*	*+7.7%*	*+2.4%*	*+1.9%*	*+5.6%*	*-1.8%*	*+3.0%*	*+3.4%*	*+4.2%*	*+4.1%*	*+3.4%*	*+3.1%*

Table. World-wide market for pharmaceutical prescription drugs (sources include *Frost & Sullivan* and *EvaluatePharma*).

WW Rx & OTC Sales Therapy Area (2011/18): Top 15 Categories & Total Market

		WW Sales ($bn)		WW Market Share	
	Therapy Area	**2011**	**2018**	**2011**	**2018**
1	**Oncology**	64.6	104.1	8.6%	11.1%
2	**Anti-diabetics**	34.4	58.2	4.6%	6.2%
3	**Anti-rheumatics**	37.6	45.0	5.0%	4.8%
4	**Vaccines**	24.9	39.9	3.3%	4.3%
5	**Bronchodilators**	35.6	32.2	4.7%	3.4%
6	**Anti-virals**	23.4	32.1	3.1%	3.4%
7	**Anti-hypertensives**	41.2	28.4	5.5%	3.0%
8	**Sensory Organs**	14.4	20.9	1.9%	2.2%
9	**Dermatologicals**	13.9	18.9	1.8%	2.0%
10	**Anti-hyperlipidaemics**	30.7	18.0	4.1%	1.9%
11	**Anti-coagulants**	8.1	16.8	1.1%	1.8%
12	**MS therapies**	12.5	15.1	1.7%	1.6%
13	**Anti-bacterials**	15.6	14.7	2.1%	1.6%
14	**Anti-fibrinolytics**	9.8	13.5	1.3%	1.4%
15	**Immunosuppressants**	6.8	12.6	0.9%	1.4%
	Top 15	374	470	49.6%	50.4%
	Other	380	464	50.4%	49.6%
	Total WW Rx & OTC Sales	**754**	**934**	100.0%	100.0%
Total 'Rx & OTC Sales' include:					
	WW Generic Sales	**65.0**	**96.3**	8.6%	10.3%
	OTC Pharmaceuticals	**37.9**	**49.2**	5.0%	5.3%

Rx : Prescription Drugs
OTC: Over-the-counter Drugs

Table. World-wide market for pharmaceutical drugs within top therapy areas (sources include *Frost & Sullivan* and *EvaluatePharma*).

In the early 1980s, the first drug, Tagamet, achieved the US$ 1 billion sales mark (definition of a blockbuster drug); today there are over 60 blockbuster drugs. The development of more personalized medicine and more segmented markets may lead to a new market situation, where less pharmaceutical drugs will obtain blockbuster status in future. The benefits of personalized medicine are an expected better treatment of more patients.

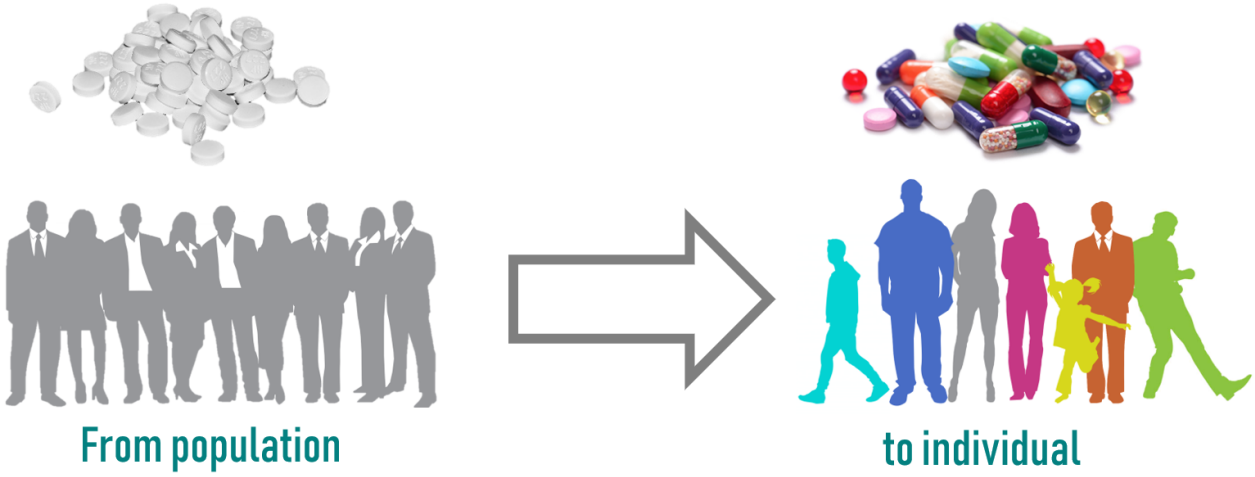

Figure. The transition to an individualised medicine market.

Commercial perspectives on pharmaceutical drug development

Several factors have caused a decline in R&D output in the pharmaceutical industry.
First, drug discovery has relied much more on new genomic screening strategies in the recent past. A myriad of new targets has been found this way, but these targets are not clinically validated and thus have had a much higher failure rate than existing targets (perhaps 50%).
Second, regulatory obstacles have been increasing. FDA have reviewed their approval policy and implemented tougher regulatory requirements, increasing the cost of drug development.
Third, the landscape in drug development is changing. Treatment are getting more efficacious and numerous. With more than 5.000 companies in drug development to date, competition is fiercer; it requires better drugs to build a successful pipeline today than 20 years ago.

A number of factors may on the other hand act as growth drivers for the pharmaceutical companies including:

- *Demographics (ageing population) to drive strong underlying demand*
- *Innovation to address unmet medical needs*
- *Rising importance of emerging markets*
- *Medicines are cost effective and help contain overall healthcare spend.*

Pharmaceutical companies adopt different strategies for competing in the market. Some companies develop drugs against new targets, a strategy which typically face high attrition risks but may lead to premium prices of successful drugs, especially if they are targeting diseases with a high mortality such as

certain cancer forms. Some companies develop second generation products of existing drugs on the market with improved features in relation to efficacy, safety and/or convenience. These drugs face less attrition but may have more difficulties in getting premium prices. Some companies aim for rare diseases with relatively few patients, but where public authorities historically have accepted to reimburse very high drug prices. Most companies try to expand the number of disease indications relevant for their approved pharmaceutical drugs. Some companies focus on the production of cheap copies of pharmaceutical drugs, generic small molecule drugs or biosimilar biopharmaceutical drugs. These drugs are priced much lower than the original drugs but have no attrition and low development expenses and short development timelines. Public authorities may in future prioritise to reimburse pharmaceutical drugs in relation to individual treatment outcomes in future. This development will stimulate more companies to develop personalized medicine. This medicine, such as the Herceptin monoclonal antibody for treatment of certain forms of breast cancer, will address a smaller patient segment compared to more generalized treatments However, such personalized medicine is expected to be much effective in the treated patients compared to more generalized treatments.

References and information sources

Shah K.K., Mestre-Ferrandiz J. and Towse A. A review of health technology appraisals: case studies in oncology. International Journal of technology assessment in health care vol 29, 101-109, 2013.

Web information available includes:
Company databases: Orbis, Compustat
Market research and industry reports produced by many companies including Frost & Sullivan and Evaluate.
Press releases, company websites, annual reports (for public firms)
Conferences and industry events
Industry experts