



## Project Portfolio Management at XYZ Pharma

Early morning, Monday 29<sup>th</sup> August 2005. John Smith, head of portfolio management and strategic planning, was paging through the slides he had prepared for the Portfolio Management Board (PMB) meeting which would start at 9 am, and which was scheduled to last until Friday. “We have been preparing this meeting for weeks”, he thought, “and it seems the PMB has some tough decisions to make”.

The PMB of XYZ Pharma, the pharmaceutical division of XYZ, one of the world’s leading companies in the life science sector, convenes yearly in August to review the composition of the research and development (R&D) project portfolio. It also meets on a monthly basis to monitor the project portfolio and make decisions regarding new developments. According to John Smith, “The PMB is an important decision making body because it shapes the future of the company by determining its product pipeline”.

The PMB members include the CEO of XYZ, the CEO of XYZ Pharma, the heads of the different business units, the heads of Development, Research, Global Marketing and Strategic Planning, the regional heads for the US, Europe and Japan and the functional managers for Regulation, Clinical, Licensing, Technical Research and Development, and Patents.

The portfolio group, led by John Smith, had analysed the project portfolio carefully and had highlighted several potential threats that required action. According to John, “There will be an in-depth discussion of which projects will be allocated additional resources, and at expense of which other projects this will be”.

### The Pharmaceutical Industry

The lion share of the pharmaceutical market is captured by approximately hundred manufacturers, which account for more than 90% of global sales. Exhibit 1 contains the top twenty pharmaceutical companies ranked by sales. Since the mid-1980s, the pharmaceutical industry has been characterized by large and frequent mergers and acquisitions (see Exhibit 2), which have had a dramatic impact on the pharmaceutical landscape. Nevertheless, each pharmaceutical “giant” only holds a relatively small share of the total drug market.

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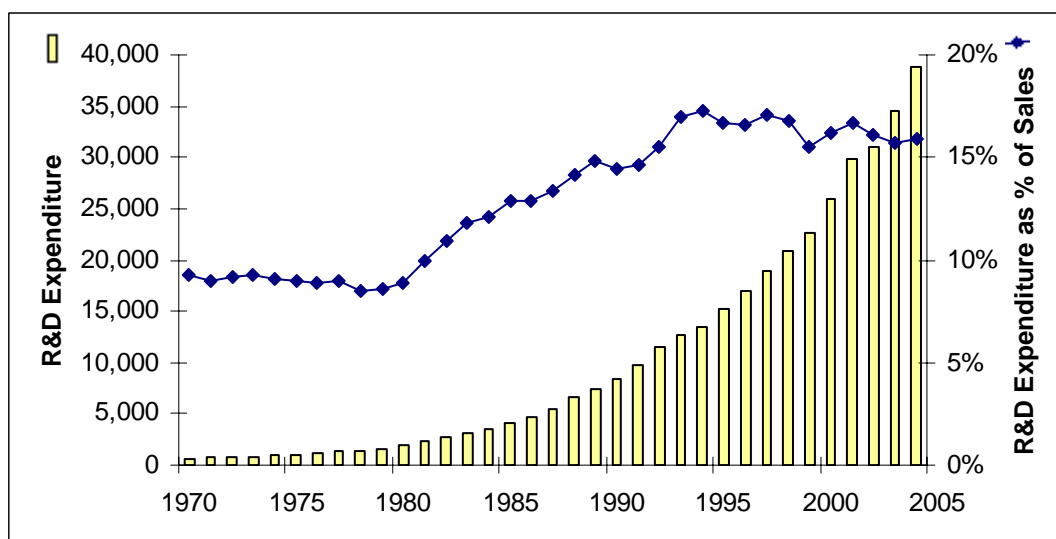
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The pharmaceutical market is characterized by increasing competition between brand-name drugs, illustrated by the shrinking time span in which a drug is the sole drug for a specific therapeutic class. Also, the profitable lifetime for drugs has substantially decreased over the last decade, largely due to quick approvals of generic copies of brand-name drugs, virtually eliminating the time lag between patent expiration and entry of generic competitors into the market.

The pharmaceutical industry is increasingly multinational in scope, with most research-based companies marketing products globally. Approximately 47% of R&D is performed in the United States, followed by Japan with 13%, the United Kingdom with 9%, France with 8% and Germany with 7% (see Exhibit 3). Approximately 45% of drugs developed are from U.S. origin, 14% originated from the U.K., 9% from Switzerland, 7% from Germany and Japan and 5% from Belgium (see Exhibit 4). The US is by far the largest market, accounting for almost half of global sales, which totalled \$550 billion in 2004 (see Exhibit 5).<sup>1</sup>

### The Drug Development Process

Drug discovery and development is an extremely risky, time-consuming and expensive process. The average time from compound to market has grown from 8.1 years in the 1960s, to 11.6 years in the 1970s, to 14.2 years in the 1980s and 1990s.<sup>2</sup> Lengthening development times also increase development costs. Recent estimates indicate that the cost of developing a medicine is around \$800 million<sup>3</sup>, significantly higher when compared to 1990, due to a substantial increase in important cost drivers such as the number of required clinical trials and patients per trial. This has resulted in a doubling of development costs since 1991, and a threefold increase since 1980. In contrast, the cost of demonstrating bio-equivalence of a generic product, the key requirement for approval of a generic drug, is currently estimated at \$1 million<sup>4</sup>. Global R&D expenditures by research-based pharmaceutical companies is estimated at around \$40 billion in 2001, increasing at around 15% per year (Figure 1). As a percentage of sales, R&D expenditures have risen from around 11% in the 1970s to approximately 16% in 2004.<sup>5</sup>



**Figure 1.** Worldwide R&D Expenditures (\$ millions, inflation adjusted)

<sup>1</sup> *The Pharmaceutical Market Outlook to 2015: Implementing innovative, long-term strategies for sustainable future growth*, Business Insights (citing IMS), May 2005.

<sup>2</sup> Joseph A. DiMasi, Director of Economic Analysis, Tufts Center for the Study of Drug Development, Tufts University, Boston, Massachusetts, testimony before the House Committee on Commerce, Subcommittee on health and the Environment, 105th Congress, 1st Session (April 23, 1997).

<sup>3</sup> *A Methodology for Counting Costs for Pharmaceutical R&Ds*, Tufts Center for the Study of Drug Development, Nov. 2001.

<sup>4</sup> Barfield, C.E. and C. Beltz, *Balancing and Rebalancing the National Interest in the Patent System*, American Enterprise Institute, Oct. 1995.

<sup>5</sup> *Pharmaceutical Industry Profile 2004*, PhRMA, Pharmaceutical Research and Manufacturers of America.

Newly developed drugs are protected by patents, providing pharmaceutical companies with the opportunity to recuperate their investments and create profits during a period of market exclusivity. Typically, 20-year patents are granted, although in general this results in a post-approval patent life of approximately 12 years. After a patent has expired, generic drugs identical to the newly developed drug can be freely sold without the need for extensive clinical trials.<sup>6</sup>

The drug registration process is heavily regulated. Stringent scientific procedures have to be followed to ensure patient safety in distinct stages, including pre-clinical and clinical tests, before a medicine can be approved for production and marketing. The drug development process in the United States is monitored by the U.S. Food and Drug Administration (FDA). Comparable institutions exist in other countries around the world. The EU created a pan-European equivalent, the European Agency for the Evaluation of Medicinal Products (EMA) which grants marketing authorisation for the whole EU. The US drug development and review process is typically as follows (a similar process is followed in Europe).<sup>7</sup>

**Basic Research (approximately 2 years)** In this phase, numerous compounds are synthesized, extracted and tested in a combinatorial and iterative manner in order to discover new substances with beneficial effects. This stage lasts for about two years, costs around \$30 to \$50 million, and on average only 40 out of an initial 10,000 compounds are taken to the next stage of pre-clinical testing.

**Pre-Clinical Testing (approximately 3 years)** In this phase, drug safety and toxicology is established through animal testing, while data is also gathered on the biological effects. The development of a drug is terminated when tests suggest that it poses a significant risk for humans, especially in the areas of organ damage, genetic defects, birth defects or cancer. On average, only one in four drugs passes this phase.

**Human Clinical Trials (approximately 6 years)** Drugs for which the pre-clinical animal data does not show an unacceptable safety risk for humans, termed "Investigational New Drugs" (INDs), are then subjected to human clinical trials, the most stringent and time-consuming process, in which people are observed for adverse effects. All harmful reactions result in termination of the drug, or are incorporated in the drug's package labelling if the adverse effect is deemed acceptable. On average, one in four drugs passes this stage to move on to the FDA review. This phase entails approximately 70 clinical trials involving 4,000 volunteers, with total costs often exceeding \$200 million. It is composed of three sub-phases:

- **Phase I Safety Trials (1 year)**  
This phase involves testing highest tolerated doses and toxicity, typically done with a few dozen healthy volunteers (50-100).
- **Phase II Safety & Efficacy Trials (2 years)**  
In phase II, efficacy and long-term safety of the drug are tested with hundreds (200-300) of volunteer patients with a control group receiving placebos.
- **Phase III Long-Term Safety & Efficacy Trials (3 years)**  
Phase III is the longest and most expensive phase, where the drug is tested on thousands (more than 3,000) of volunteer patients (including elderly people, patients with multiple diseases and patients with impaired organs) for long-term safety, optimum dosage levels and more subtle adverse effects.

**FDA Review (approximately 1-2 years)** In this phase, a New Drug Application (NDA) document is submitted to the FDA with data on each treated patient, and with production plans. An NDA documents typically contains thousands of pages, and takes up to two years to review by the FDA. The FDA continues to monitor the process after approval is granted for production and marketing. On average, eight out of ten drugs make it through this phase.

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<sup>6</sup> In some countries, including Argentina, Brazil, Mexico, India, Egypt and South Africa, patent piracy, where protected drugs are copied without compensation, has sometimes been a major problem. However, many of these countries have recently tightened their patent protection to international standards.

<sup>7</sup> Based on data from the Center for the Study of Drug Development, Tufts University, 1995.

<i>Phase</i>	<i>Probability of Advancing to next Stage</i>	<i>Probability of approval</i>	<i>Proportion of Total R&amp;D Costs</i>
<b>Basic Research</b>	0.4%	0.02%	24%
<b>Pre-Clinical</b>	25%	5%	12%
<b>Clinical Phase</b>	25%	20%	29%
<b>FDA Review</b>	80%	80%	35%

**Table 1.** Probability of passing each of the drug development phases

Table 1 illustrates the high risks that are inherent to the pharmaceutical industry. On average, only one in five drugs entering clinical trials is launched on the market<sup>8</sup>. Overall, only one in five thousand developed compounds in the research phase makes it to the market. As a consequence, a large portion of all development costs are spent on drugs that never reach the market, illustrating the high *technical risks* involved. Even of the drugs that reach the market, only 30% achieve the commercial success necessary to recover the (after-tax) development costs to yield a healthy return, illustrating the additional *commercial risks* involved. Generally, the top 20% of the products with the highest revenues generate 70% of the returns. Thus, companies must rely on a limited number of highly successful products to finance their continuing R&D.<sup>9</sup> Nevertheless, pharmaceutical companies in recent years have been able to report healthy profits, of about 20% on gross revenues. Roughly, production costs account for 10%-15% of total manufacturing costs, R&D for 20%, taxes for 15%, 30% for advertising and marketing, leaving approximately 20% profit.<sup>10</sup>

### Pipeline and Portfolio Management

The top management of XYZ is committed to a vigorous growth in total sales and the creation of shareholder value. Because the global pharmaceutical industry is increasingly competitive, a constant stream of product introductions has to be maintained. “A well-managed product pipeline is essential to support sales and profits, making product or project portfolio management a crucial success factor”, says John Smith. “And because of the long R&D lead time, a good performance today is actually determined to a large extent by which decisions have been made 10 years ago.”

The XYZ Pharmaceutical product pipeline is one of the broadest in the industry and currently comprises a total of 69 projects in clinical development, and 106 projects from the pre-clinical stage onwards. According to the CEO: “XYZ’s pipeline is already one of the strongest in the industry.” He added: “We have a number of strong pipeline compounds as well as limited patent expiry exposure”.

The projects in the pipeline include both new molecular entities (NMEs) and additional indications or formulations for marketed products. Overall, there are 27 projects in late-stage development (Phase III or FDA review), to sustain mid-term growth, and 32 projects in Phase II. XYZ expects to be able to launch one or two NMEs per year and plans to introduce new products at a sustained pace.

XYZ Pharma Research is working in a wide range of therapeutic areas, in research centres all over the world. Each therapeutic area is a separate business unit, responsible for its own performance. Each of the business units is allocated a research fund from corporate headquarters, based on a commitment to contribute a certain profit to the Pharma division. Additional profits beyond the agreed value can be re-used to fund research, or can be transferred to headquarters, resulting in bonuses for the unit’s employees. Unlike some of its more focused competitors, XYZ Pharma’s products span a wide range of therapeutic areas, including immunology, inflammatory diseases, central nervous system disorders, cardiovascular, endocrine and metabolic diseases, oncology, dermatology and asthma. In recent years, however, XYZ has been focusing on both cardiovascular diseases and cancer. “This strategy has paid off”, confirmed John Smith, “We boast a strong portfolio in both those areas, driven by blockbusters for a few years to come.” However, other areas of the portfolio have

<sup>8</sup> *Industry Profile 2003*, www.phrma.org

<sup>9</sup> Henry G. Grabowski and John M. Vernon. Returns to R&D on New Drug Introductions in the 1980s, *Journal of Health Economics*, 13, 383-406, 1994.

<sup>10</sup> P. Barry, “What’s behind high drug prices in the U.S.?”, *AARP Bulletin*, 41 (4), April 2000.

suffered some setbacks: late-stage trials had to be terminated and some applications had trouble in the regulatory arena. This has hit the central nervous system unit especially hard, which is not expected to be a major growth driver anymore.

### The Portfolio Management Board

Decisions concerning the project pipeline are taken by the Portfolio Management Board or PMB. "The PMB has two important functions: At its yearly meeting in August, it decides on the shape and content of the project pipeline by accelerating and delaying projects, and, on a regular basis, the PMB checks its evolution", says John Smith. "My role is to prepare the portfolio data for these meetings, and integrate the requirements from the different business units into a single portfolio from a company perspective". Before the meeting, each of the business units submits individual business plans with capital and resource requirements based on the projects within the unit. Input from Project Teams (resources, milestones, risks), Strategic Marketing (market performance and potential revenue streams) and Strategic Planning (disease area audits and benchmarking) begins in early December. The portfolio group, led by John Smith, consolidates the business plans of the business units. "It was a hectic time this year, but we managed to finalise everything and build a provisional project budget in two weeks time to be ready for the PMB meeting", remembers John. "We needed to allow the PMB five working days to review the documentation associated with the annual strategic plan."

The yearly PMB meeting deals with an annual budget of more than US\$5 billion and considers approximately 150 projects executed in ten development sites worldwide. Its main purpose is to decide which compounds to develop and their priority. "The resulting development budget for every business unit is the basis for a contract", explains John. Any individual project can be singled out for special attention concerning its expected profitability, strategic fit and contribution to portfolio or pipeline balance. The projects are subsequently monitored by the PMB in quasi-monthly meetings, which are held to evaluate the performance of the projects against the objectives established in August.

The PMB's decision process consists of two parts (Figure 2). The preparation of the yearly business plan takes place during the planning period, from June until August, followed by the implementation and control of the plan during the budgetary year, from January to January. The planning process starts with the evaluation of the options in the light of the strategic plan and the analysis of perceived opportunities. On the basis of this information, the decision makers agree on targets and the optimal portfolio that enables them to reach their proposed objectives. These decisions are recorded in the annual business plan at the PMB meeting end of August. During the execution of the plan, milestones may be reached or opportunities and threats identified, requiring decisions to be taken. The quasi-monthly meetings are held for that purpose and allow flexible project execution.

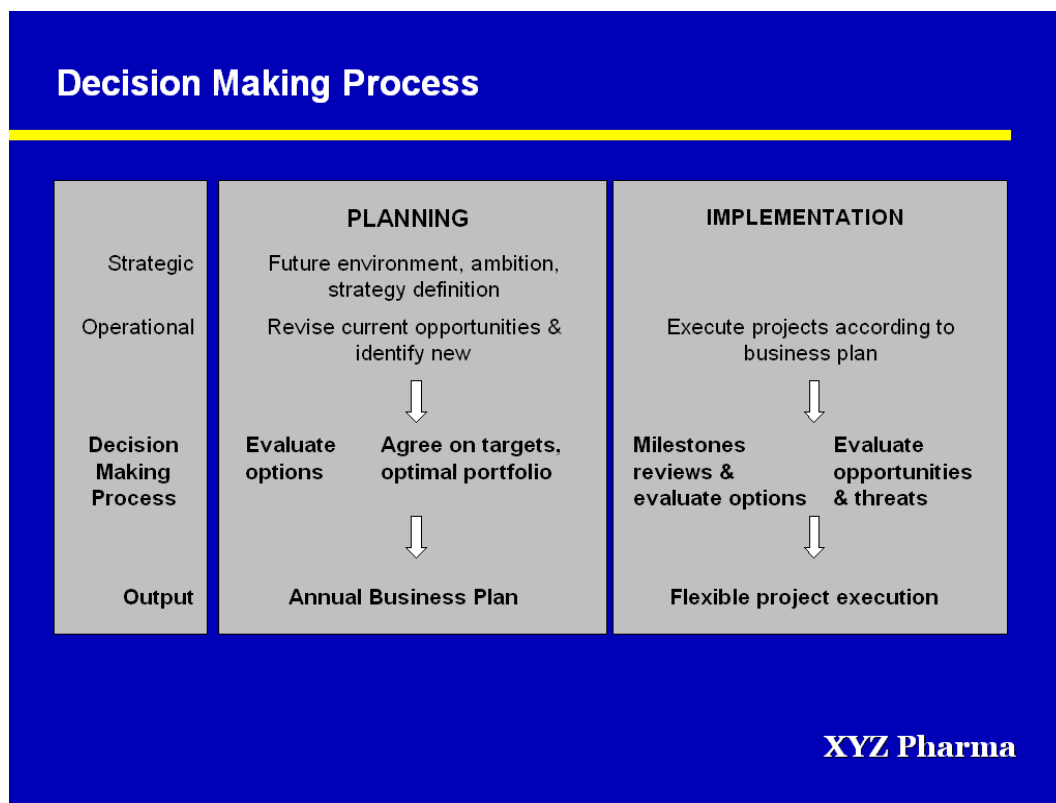


Figure 2. Representation of the Decision Making Process

### Portfolio Review Criteria

XYZ’s CEO had recently announced his expectations of double-digit growth rates for XYZ’s pharmaceutical division, which is significantly above the industry average, and one of the PMB’s main concerns was on how to reach that target. To maintain growth, XYZ needed to deliver on its pipeline and introduce new successful products, compensating for the decline in sales of mature and launched products. “Also, to sustain a continuous growth, the pipeline has to be balanced”, says John Smith. Balance is determined relative to the pipeline “fill” that is required to maintain the flow of product launches given historic attrition rates of projects in the R&D funnel. The projects in the pipeline can be subdivided into innovative and life cycle management projects, or NME versus LCM products. Though R&D into new molecular entities are less likely make it to market, the reward is typically higher, and blockbusters are usually found amongst NME projects rather than life cycle management projects.

Although XYZ’s pharmaceutical division boasts a healthy profit margin, it is heavily reliant on a few drugs that will recuperate their R&D expenses. The portfolio review group requires that all projects asking for funds be accompanied by a Net Present Value (NPV) analysis. A project’s potential value is derived from the estimation of future resource requirements, timing of the R&D stages and market launch, and the projections of sales revenues and associated marketing costs generated by the Strategic Marketing Group. The sales forecasts are made based on a number of assumptions concerning the indication and label of the drug, the disease population, the reimbursement potential of the drug, potential market share and pricing.

“Next to financial criteria, we also consider the strategic fit of any project under consideration”, says John Smith. Strategic alignment is assessed based on the strategic plan in which therapy areas of interest have been highlighted as a result of a disease area and competitor analysis. As population composition and disease prevalence change, pharmaceutical companies adapt their research focus. “This explains why many companies have been concentrating on chronic diseases such as hypertension and cholesterol control since the mid-1990s”, said John. “However, even though most

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pharmaceutical companies have a strategic focus, they cannot necessarily enforce it, because the R&D process is essentially opportunistic: funding of research in the strategic focus area does not guarantee discovery of interesting compounds.”

Pharmaceutical R&D activities are subject to a high level of risk, which is an essential ingredient of all the reports presented to the PMB: project values are expressed as expected values, weighted with the probabilities of reaching the successive stages and ultimately the market. According to John, “In PMB meetings, we only discuss expected values, e.g. expected sales or expected NPV. It is meaningless to talk about a potential 5 billion drug without taking into account the probability of the drug ever reaching the market. Unfortunately, there is little that can be done about the technical success or failure of a project. Requiring a higher success probability before starting a project would effectively rule out most projects, especially NMEs. Hence we rely on portfolio diversification. However, it is essential that we monitor the risk in the portfolio, making sure that any decision taken results in acceptable risk limits.”

Next to technological risks, XYZ Pharma also faces considerable uncertainty about the sales that the product will generate once launched. Initial projections are made for a distant future when the compounds characteristics are still relatively unknown. A typical NPV valuation is presented in Exhibit 6, in the format used by XYZ’s portfolio group. The cash flows are discounted using a company-wide weighted average cost of capital (WACC).

### The Meeting

At the start of the meeting, the portfolio management group, represented by John Smith, presented a summary of the current state of the project portfolio and pipeline. Some of the presented slides are given in Exhibit 7. Slide 1 shows the number of current projects in each phase in the different business units. Slide 2 shows the expected NPV per phase in the different business units (in \$millions). Slide 3 graphs the number of expected launches for the next 10 years. These figures take into account the probability to market of each of the drugs due to be launched in that year.

Slide 4 presents an overview of the net present value of all the projects in each business unit, represented by a cumulative probability distribution. The distributions show the likelihood of a particular net present value based on the technical success of the projects in the portfolio. For instance, Slide 4 shows that the net present value of the projects in therapy area 2 (the curve on the right) is between approximately \$3 billion and \$13 billion, and shows that the probability of a net present value of at least \$7.5 billion is around 70%.

Several slides show the expected sales and sales growth, based on the median sales figure. John Smith commented: “We need to look at ranges when forecasting sales, instead of just focusing on the most likely sales figure. However, this is a major challenge for the marketing group.” The decomposition of expected sales into therapeutic area, project type or brand name is also communicated. The major drugs together account for about 40% of the sales of XYZ for the next 5 to 7 years, and John Smith claims that “[this] means that XYZ is more diversified than most of the other major pharmaceutical companies”.

XYZ is also looking into the respective sales of LCM and NME projects, and of General Practitioner (GP), Niche and Specialized products (Slides 5 and 6). John Smith adds: “Because our current blockbusters are pretty strong, they allow for interesting line extensions. However, XYZ also has other promising NME projects due to be released in the next 5 years, especially in the cardiovascular therapy area and the immune disorder and inflammation franchise.” GP products account for the majority of sales, but have a relatively low profitability, whereas Niche and Specialized products offer higher profitability for a smaller sales potential. Different type of products might also react differently to patent expiry: GP products are usually copied very quickly and market share loss can be severe.

Several slides contain financial information for each of the projects, such as NPV, expected NPV, peak sales and expected contribution to sales growth, as in Slide 7. As John Smith explained: “Last year was the first time they made decisions heavily based on financials”.

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Based on the information contained in the previous slides, the decision makers assign projects to three different categories: Heavyweight projects, Key projects and Foundation projects. Heavyweight projects are typically close to market and have blockbuster potential, and have a high priority for accessing resources. Key projects are also important to the company and have potential, but are still far away from market. The Foundation projects comprise the bulk of the portfolio. If the budgetary requirement to continue all the projects in the portfolio exceeds the available funds, some projects are put on hold.

On Friday evening, John, exhausted, reflected back on the past week. The PMB meeting had decided on the route to take for the next year, with some projects put on hold and others pushed centre-stage. Despite the long discussions and lively debates, John felt it was a productive week, and that the decisions made by the PMB would gain support throughout the organization.



Exhibit 1 Top 20 Pharmaceutical Companies by Sales (in US\$ millions)<sup>11</sup>

Rank	Company	Country	Sales (\$ billion)	Share of World Market
1	Pfizer	US	46.13	8.39%
2	GlaxoSmithKline	UK	31.42	5.71%
3	Sanofi-Aventis	France	29.60	5.38%
4	Johnson & Johnson	US	22.13	4.02%
5	Merck	US	21.49	3.91%
6	AstraZeneca	UK	21.43	3.90%
7	Novartis	Switzerland	18.50	3.36%
8	Bristol-Myers Squibb	US	15.48	2.81%
9	Roche	Switzerland	13.84	2.52%
10	Eli Lilly	US	13.06	2.37%
11	Wyeth	US	13.02	2.37%
12	Abbott Laboratories	US	11.46	2.08%
13	Amgen	US	9.98	1.81%
14	Takeda	Japan	8.54	1.55%
15	Boehringer Ingelheim	Germany	7.67	1.39%
16	Schering-Plough	US	6.42	1.17%
17	Bayer	Germany	5.53	1.01%
18	Novo-Nordisk	Denmark	4.85	0.88%
19	Schering AG	Germany	4.17	0.76%
20	Sankyo	Japan	4.15	0.75%

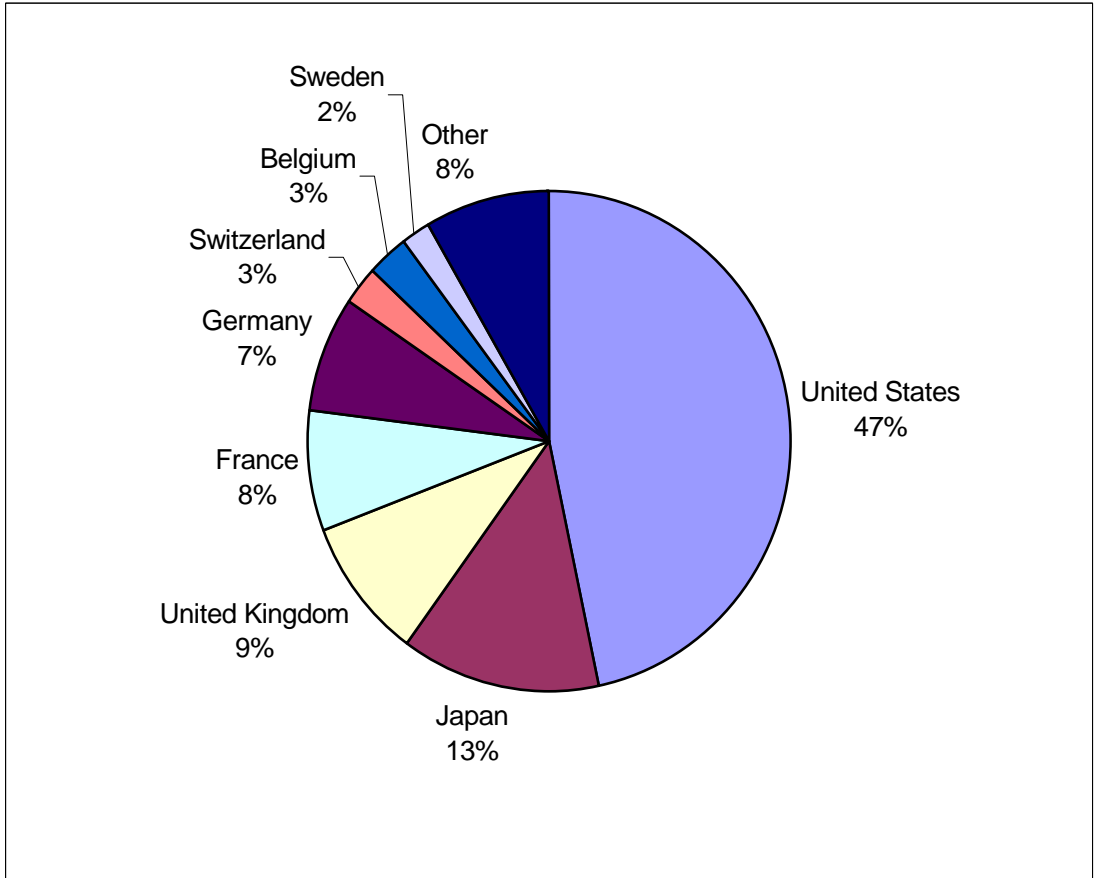
<sup>11</sup> 2005 Top Companies (based on 2004 pharma revenues, in millions), <http://www.contractpharma.com>, July/August 2005.

Exhibit 2 Mergers and Acquisitions in the Pharmaceutical Industry<sup>12</sup>

<b>Year</b>	<b>Company 1</b>	<b>Company 2</b>	<b>New Name</b>
2005	Vicuron Pharmaceuticals Inc	Pfizer	
2005	Fournier Pharma	Solvay SA	
2005	Hexal AG	Novartis	
2005	Fujisawa Pharmaceutical Co Ltd	Yamanouchi Pharmaceutical Co	Astellas
2004	Sanofi-Synthelabo	Aventis	Sanofi-Aventis
2004	SICOR Inc	Teva Pharma Inds Ltd	
2003	Scios Inc	Johnson & Johnson	
2003	Pharmacia Corp	Pfizer Inc	
2002	Lek(Slovenia)	Novartis AG	
2001	DuPont Pharmaceuticals Co	Bristol-Myers Squibb Co	
2001	ALZA Corp	Johnson & Johnson	
2001	BioChem Pharma Inc	Shire Pharmaceuticals Grp PLC	
2001	Knoll AG(BASF AG)	Abbott Laboratories	
2000	G.D. Searle (Monsanto)	Pharmacia & Upjohn	Pharmacia Corporation
2000	SmithKline Beecham PLC	Glaxo Wellcome PLC	GlaxoSmithKline
2000	PathoGenesis Corp	Chiron Corp	
2000	Jones Pharmaceutical Inc	King Pharmaceuticals Inc	
2000	Warner-Lambert Co	Pfizer Inc	Pfizer Inc
2000	Liposome Co Inc	Elan Corp PLC	
2000	-	Pasteur-Merieux Connaught	Aventis Pasteur
2000	Centecor	Johnson & Johnson	
1999	Genentech Inc	Roche Holding AG	
1999	Agouron Pharmaceuticals Inc	Warner-Lambert Co	
1999	Hoechst	Rhone-Poulenc Rorer	Aventis AG
1998	Astra	Zeneca	AstraZeneca
1998	Sanofi	Synthelabo	Sanofi-Synthelabo
1998	Corange Ltd	Roche Holding AG	
1997	Boehringer Mannheim	Hoffman-La Roche	
1997	Amersham	Nycomed	
1996	Ciba-Geigy	Sandoz	Novartis AG
1996	Athena Neurosciences Inc	Elan Corp PLC	
1995	Hoechst-Roussel	Marion Merrell Dow	
1995	Pharmacia	Upjohn Co	Pharmacia & Upjohn
1995	Fisons PLC	Rhone-Poulenc Rorer Inc	
1995	Boots	Knoll	
1995	Wellcome PLC	Glaxo Holdings PLC	Glaxo Wellcome
1994	American Cyanamid	American Home	
1994	Erbamont	Pharmacia	
1994	Syntex Corp	Roche Holding AG	
1994	Sterling (prescription)	Sanofi	
1994	Sterling Winthrop Inc	SmithKline Beecham PLC	
1991	SmithKline	Beecham	SmithKline Beecham
1990	Kabi	Pharmacia	
1990	Rorer	Rhone-Poulenc	Rhone-Poulenc Rorer
1989	Squibb	Bristol-Myers	Bristol-Myers-Squibb
1989	Merrell-Dow	Marion	Marion Merrell Dow
1988	Kodak	Sterling	
1986	Key	Schering-Plough	

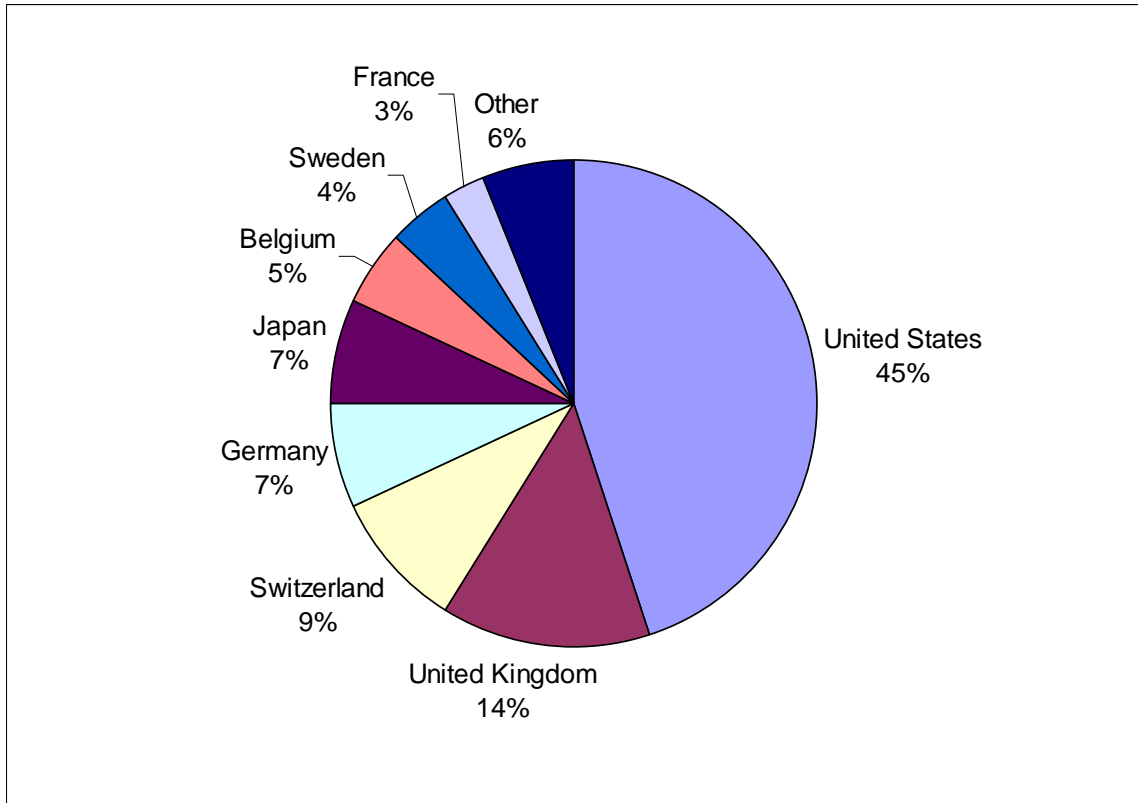
<sup>12</sup> Windhover's Health Care Strategist, 2000 + Thomson Deal Database.

Exhibit 3 Pharmaceutical R&D by Country<sup>13</sup>



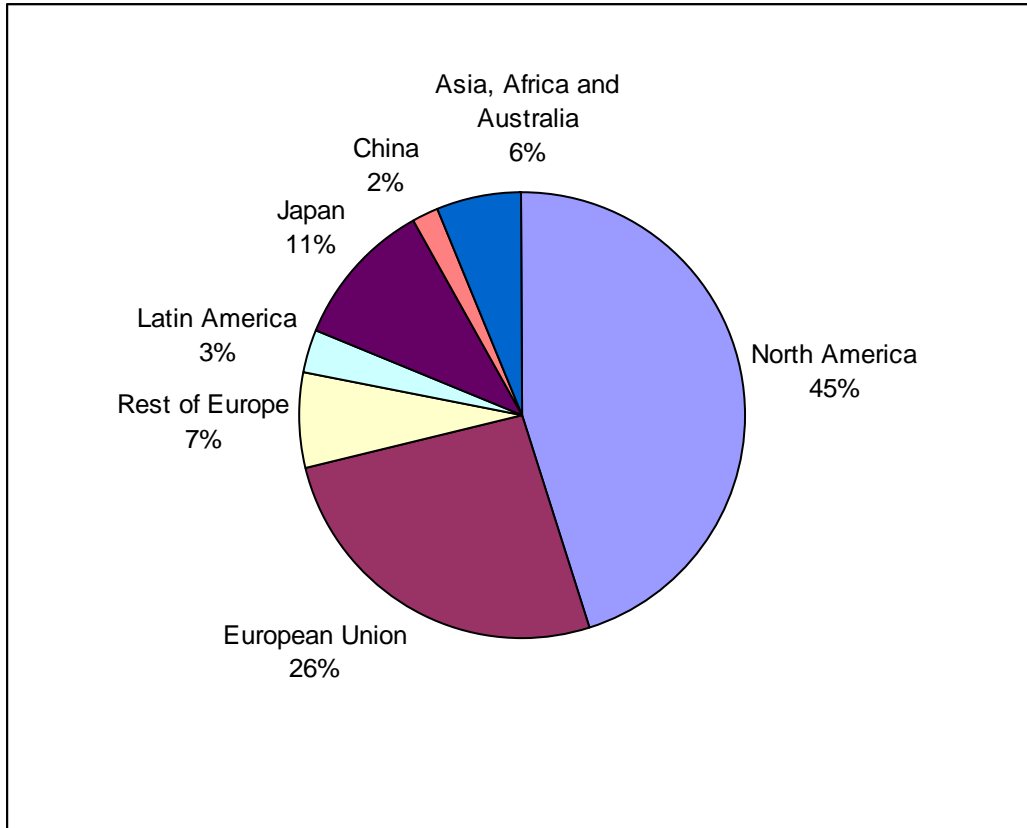
<sup>13</sup> The Pharmaceutical Industry in Figures, Key Data - 2005 update, EFPIA (2005).

Exhibit 4 Drugs Introduced per Country<sup>14</sup>



<sup>14</sup> Barral, PE. *20 Years of Pharmaceutical Research Results Throughout the World*. Rhone-Poulenc Rorer Foundation, 1996

Exhibit 5 World Pharmaceutical Market<sup>15</sup>



<sup>15</sup> *The Pharmaceutical Market Outlook to 2015: Implementing innovative, long-term strategies for sustainable future growth*, Business Insight, May 2005.

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Exhibit 6 NPV Calculations of Projects

Discount Rate	10.00%
G&A Rate	2.00%
Distribution	1.00%
Tax Relief	25.00%
Work Capital	15.00%
Base Year	1-Jan-06
<b>Product Type</b>	
GP	20.00%
Niche	15.00%
Specialised	10.00%

General & Administrative expenses (as a percentage of gross sales)  
 Distribution cost (as a percentage of gross sales)  
 The net contribution is taxed at 25%  
 All cash flows are discounted to the base date  
 General Practitioner Product  
 Niche Product  
 Specialised Product

Compound XYZ001<sup>a</sup>

Stage: Pre-Clinical

Budget Status: Active

GP/ Spec: GP

Launch Year		2012	Post Launch Expenses (Value)				Pre Launch Expenses(Value)							
Year	Probability of cash flow <sup>b</sup>	Gross Sales	Cost of Goods Sold (COGS)	Marketing & Sales (M&S)	Royalties	Milestones	Total Product Costs including distribution <sup>c</sup>	Contribution after G&A and revenue deduction <sup>d</sup>	Internal R&D Cost	External R&D Cost	Phase 4 Estimates	Other Dev Costs	Free Cash Flow <sup>e</sup>	Free Cash Flow after tax <sup>f</sup>
	%	Value												
2006	91.2%	0.00							3.13	0.74			-3.87	-2.90
2007	28.4%	0.00							6.16	5.40			-11.56	-8.67
2008	18.3%	0.00							14.94	18.76			-33.70	-25.28
2009	12.7%	0.00							28.32	39.04			-67.35	-50.52
2010	9.9%	0.00							8.17	9.80			-17.97	-13.48
2011	8.7%	0.00		86.73			86.73	-86.73	1.92	2.31			-90.97	-68.23
2012	7.1%	144.56	26.02	260.20			287.67	-146.00					-146.00	-109.50
2013	7.0%	289.12	52.04	505.95			560.88	-277.55					-277.55	-208.16
2014	7.0%	491.50	88.47	491.50			584.88	-103.21					-103.21	-77.41
2015	7.0%	737.24	132.70	442.35			582.42	140.08					140.08	105.06
2016	7.0%	1069.73	192.55	427.89			631.14	417.19					417.19	312.90
2017	7.0%	1445.58	260.20	433.67			708.33	708.33					708.33	531.25
2018	7.0%	1445.58	260.20	289.12			563.78	852.89					852.89	639.67
2019	7.0%	1445.58	260.20	216.84			491.50	925.17					925.17	693.88
2020	7.0%	1329.93	239.39	132.99			385.68	917.65					917.65	688.24
2021	7.0%	1130.44	203.48	113.04			327.83	780.01					780.01	
2022	7.0%	0.00												
2023	7.0%	0.00												
2024	7.0%													

NPV<sup>g</sup> **751.54**  
 NPV with TV<sup>h</sup> **1175.92**  
 eNPV **72.64**

<sup>a</sup> The first line contains: compound name, current stage, budget status (active = included in the budget) and product type.

<sup>b</sup> Because the success of each stage is uncertain, cash flows occur with a probability. The probabilities are given per stage and are converted into yearly probabilities by taking a weighted average of the probabilities of the stages occurring within the year.

<sup>c</sup> Includes COGS, G&A expenses, royalties and distribution cost (1% of gross sales).

<sup>d</sup> Gross sales minus total product costs minus G&A cost (2% of gross sales).

<sup>e</sup> Contribution after G&A and revenue deduction minus the cost of R&D.

<sup>f</sup> Free cash flow with a tax burden (or relief) of 25%.

<sup>g</sup> Computed as if all cash flows after tax were certain and includes sales for the first 9 years.

<sup>h</sup> Assumes that the sales after the 9<sup>th</sup> year decay at a constant rate determined by the product type (TV = terminal value).

Exhibit 7 PMB Meeting Slides

### Projects per Therapy Area

	Pre-Clinical	Phase I	Phase II	Phase III	Regulation	Launched
TA 1	4	1	5	8	2	5
TA 2	10	4	4	4	0	7
TA 3	6	2	7	2	1	7
TA 4	2	6	5	3	0	13
TA 5	5	0	3	1	2	4
TA 6	4	5	6	1	1	4
TA 7	6	0	2	0	2	5

**XYZ Pharma**

Slide 1. Projects per Therapy Area

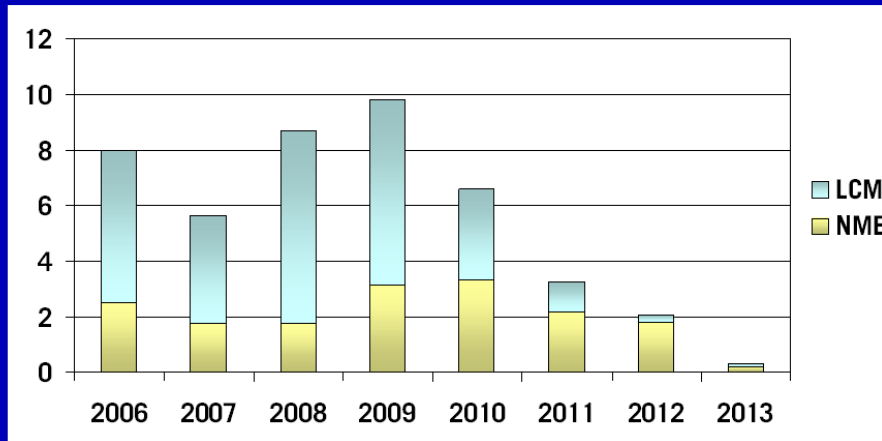
### Expected NPV per Therapy Area (in mio \$)

	Pre-Clinical	Phase I	Phase II	Phase III	Regulation	Launched
TA 1	449	9	1,194	2,446	933	15,074
TA 2	726	530	1,472	5,795	0	1,345
TA 3	229	462	1,411	213	417	3,805
TA 4	63	712	2,493	1,831	0	23,640
TA 5	1,051	0	432	25	413	721
TA 6	338	899	2,201	602	404	5,728
TA 7	152	0	491	0	1,911	2,218

**XYZ Pharma**

Slide 2. Expected NPV per Therapy Area

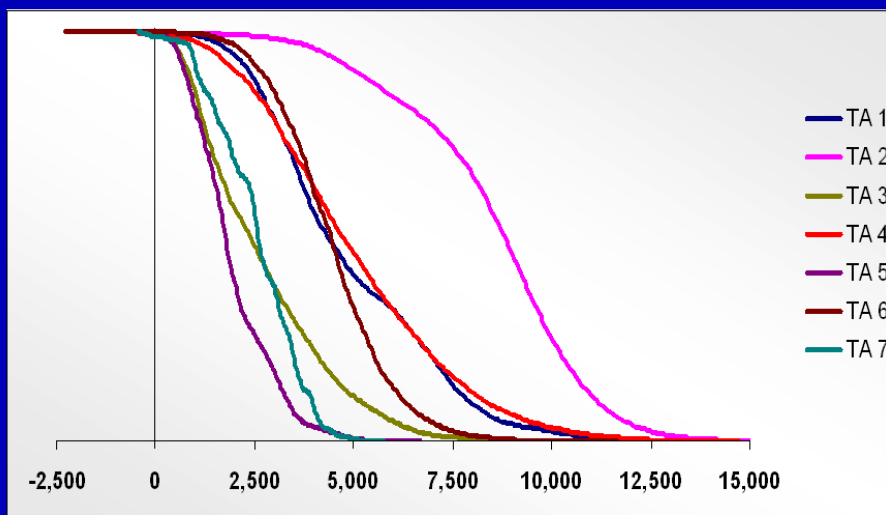
## Probabilized Launch Schedule



XYZ Pharma

Slide 3. Expected Launches until 2010

## Cumulative Probability Distribution per Therapy Area<sup>1</sup>



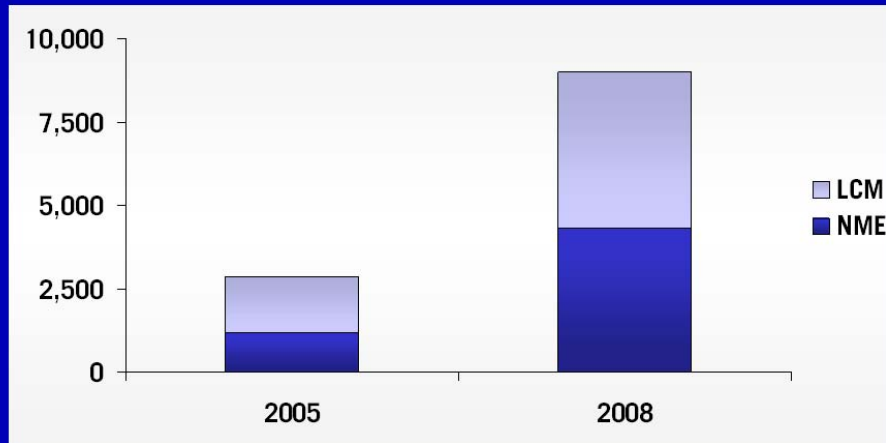
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<sup>1</sup> Exclusive launched products

Slide 4. Cumulative Probability Distribution per Therapy Area



### Percentage NME versus LCM expected sales<sup>1</sup>

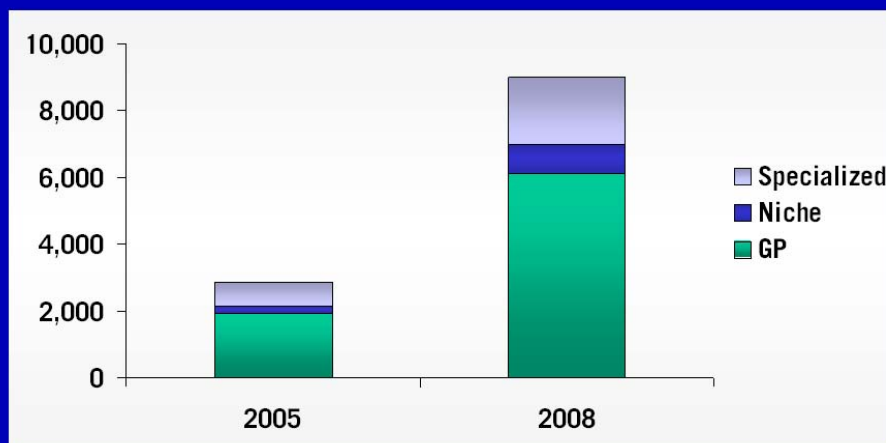


<sup>1</sup> Exclusive launched products

XYZ Pharma

Slide 5. Composition of Expected Sales: NME versus LCM

### Percentage of General Practitioner, Niche and Specialized Products in expected sales<sup>1</sup>



<sup>1</sup> Exclusive launched products

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Slide 6. Composition of Expected Sales per Product Type

## Financial Information on the projects (in mio \$)

TA	Project	NPV	Expected NPV	Peak Sales	Expected Sales Growth
TA 1	Project 31	1,019	574	520	165
TA 1	Project 32	827	693	296	145
TA 1	Project 33	54	16	53	34
TA 1	Project 34	286	255	340	144
TA 1	Project 35	1,029	774	313	99
TA 1	Project 36	203	181	245	123
TA 1	Project 37	666	22	837	505
TA 1	Project 38	3,566	1,044	2,177	2,177
TA 1	Project 39	2,707	260	3,249	1,962
TA 1	Project 40	3,351	152	2,436	2,174
...	...	...	...	...	...
TA 7	Project 166	863	311	658	522
TA 7	Project 167	502	43	486	465
TA 7	Project 168	889	50	1,020	153
TA 7	Project 169	1,167	1,046	446	317
TA 7	Project 174	107	4	102	65

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**Slide 7.** Financial information on the projects