Business Models & Portfolio Management in the Pharmaceutical Industry

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Summer 2016

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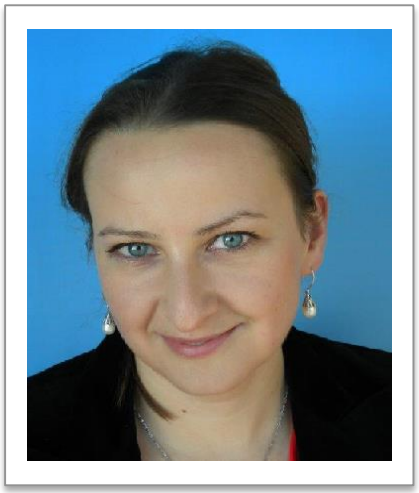
To give you a quick background about myself



EMLYON business school

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Objective of the lecture

Gain a helicopter view of the money flow in the pharmaceutical industry

- 1st Part : Understand the **Top 3 business models** in the pharmaceutical industry
- 2nd Part : Understand the **3 key strategies to refuel the pipeline**
- 3rd Part : Understand **how to prioritize compounds within the portfolio**

Agenda

1. **The pharma business models**
2. How to refuel the pipeline
3. Prioritize the best compounds within your ideal portfolio

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Overview of the 3 major business models :
Innovator, Generic, and OTC

Innovator

- New Chemical Entities (NCEs)
- New Biological Entities (NBEs)
- High R&D investment
- Revenue from compound only guaranteed when patents valid

Generic

- After innovator's patents have expired, the generic company can make the copy
- The generic is cheaper because clinical data from the innovator can be re-used
- Price discount : 10% to 95%

OTC

- Based on generic drugs with a very safe product profile
- Patient can obtain the drug without prescription
- Branded generics (e.g. Advil)
- Direct-to-consumer marketing

Before we review in details the above 3 models, what other models exist in the pharma industry ?

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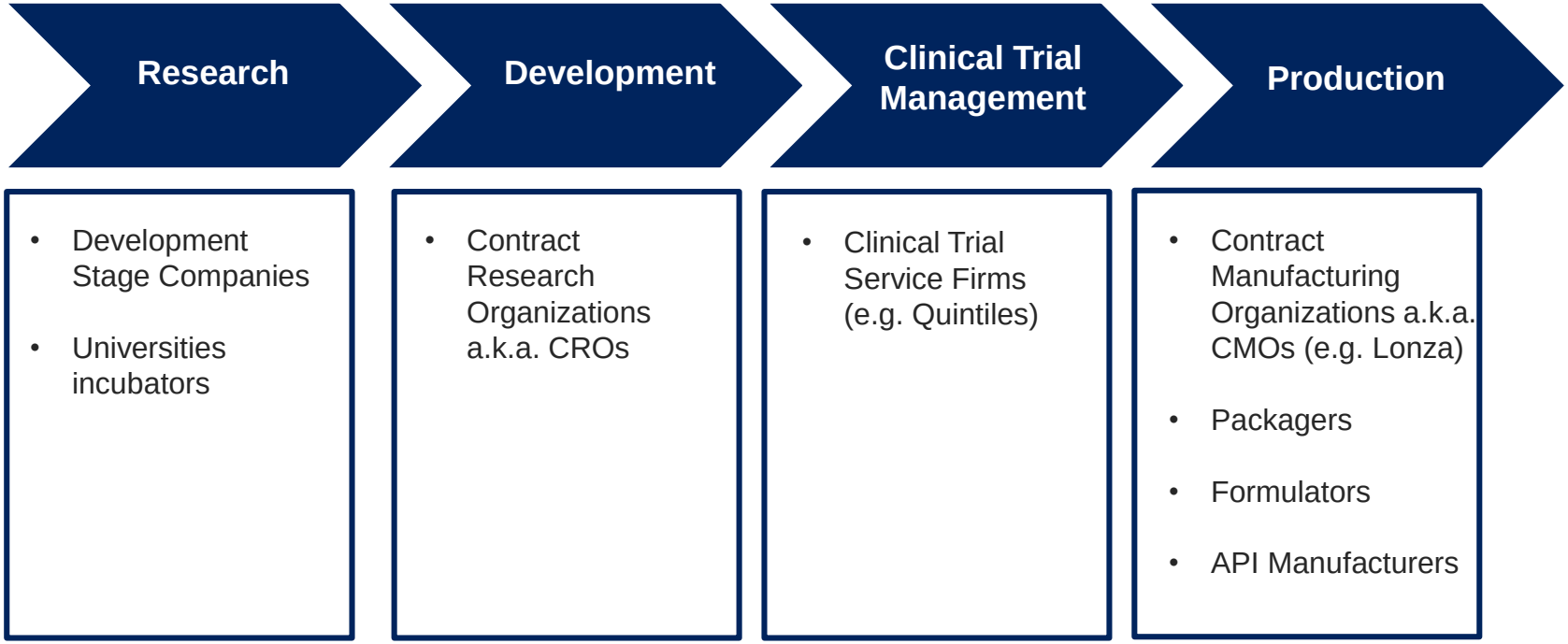
All other business models in the pharma industry gravitate around the Top 3

Let's look how external players map along the pharma value chain



Hence, it is key to understand the major 3 business models … starting with Innovator model

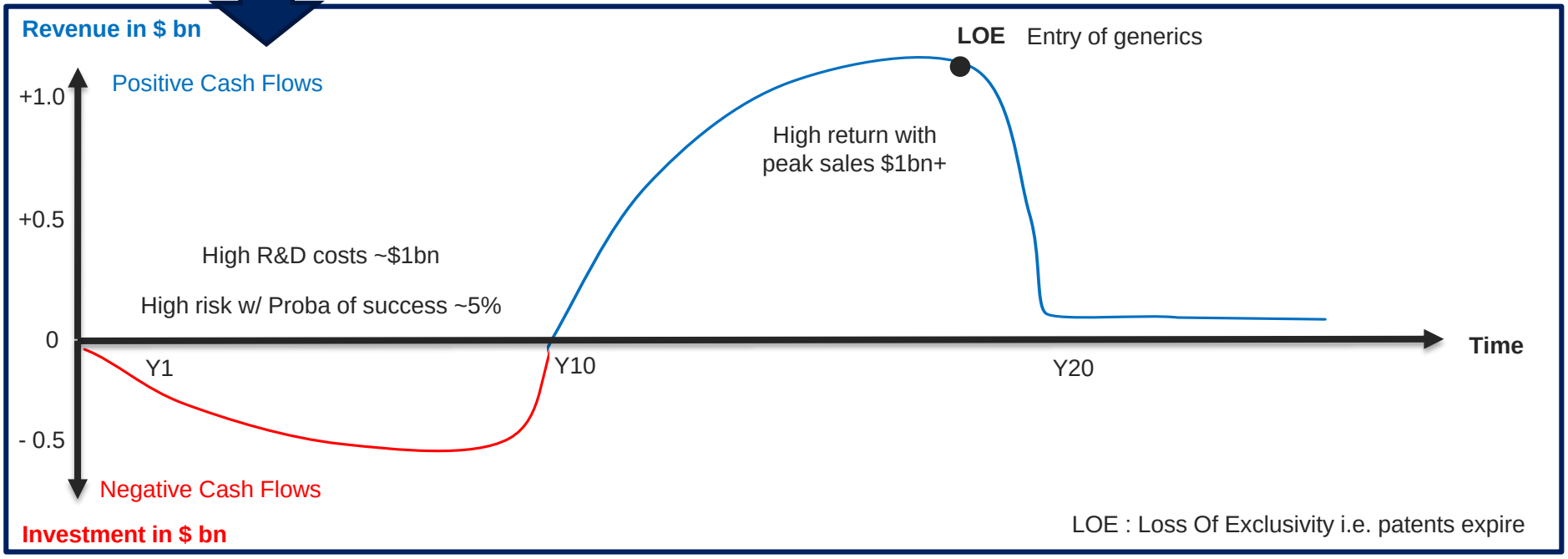
Source : Innovative Business Models in the Pharmaceutical Industry: A Case on Exploiting Value Networks to Stay Competitive by Francesca Capo, Federica Brunetta and Paolo Boccardelli

Innovator business model

Innovation based

Strategy

- The strategy is innovation based
- Sales are function of patent life cycle
- Need to constantly refuel pipeline b/c LOE - generic player may take up to 90% of your sales in 6 m



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Let's look at a real life example

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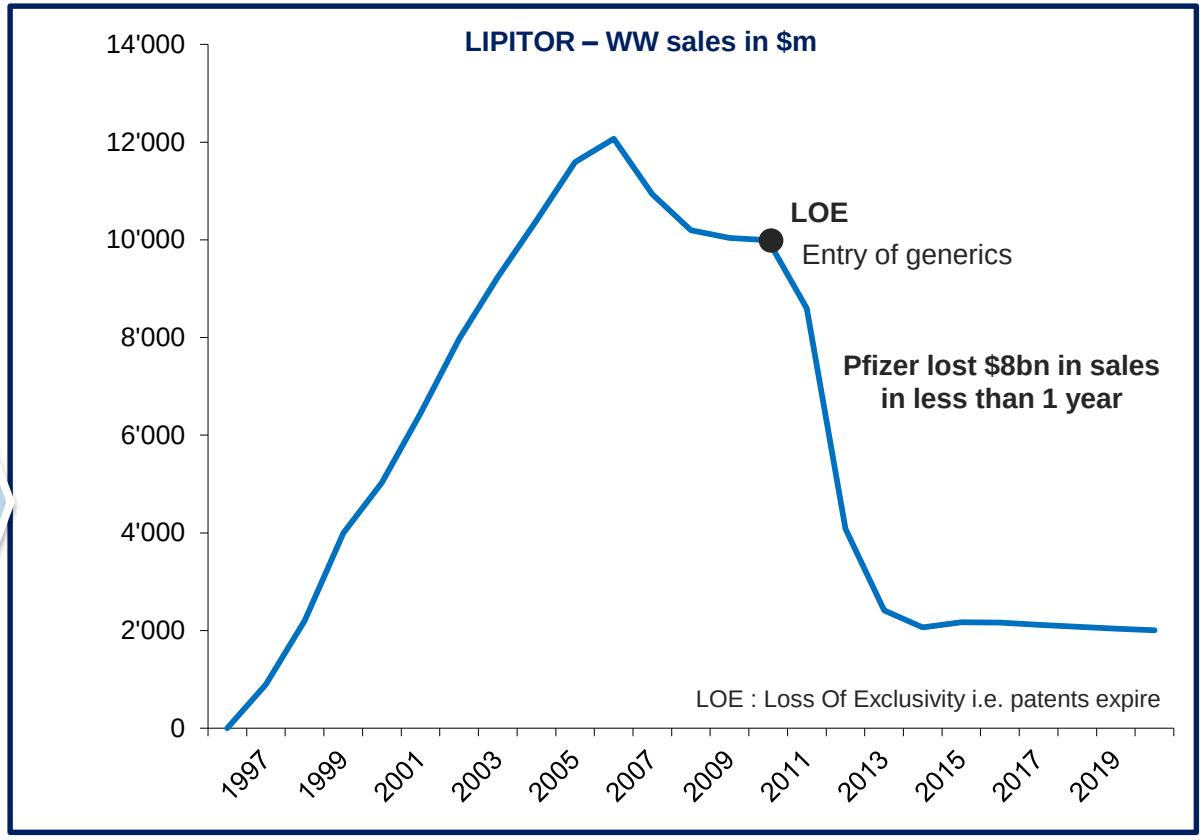
Innovator business model
Lipitor case

- Brand : Lipitor
- Company : Pfizer
- INN : atorvastatin
- Class : cholesterol-lowering agent
- Launched in 1997
- World's bestselling drug of all time
- Peak sales : $12bn



Source : Evaluate Pharma, http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(11)61858-8/fulltext

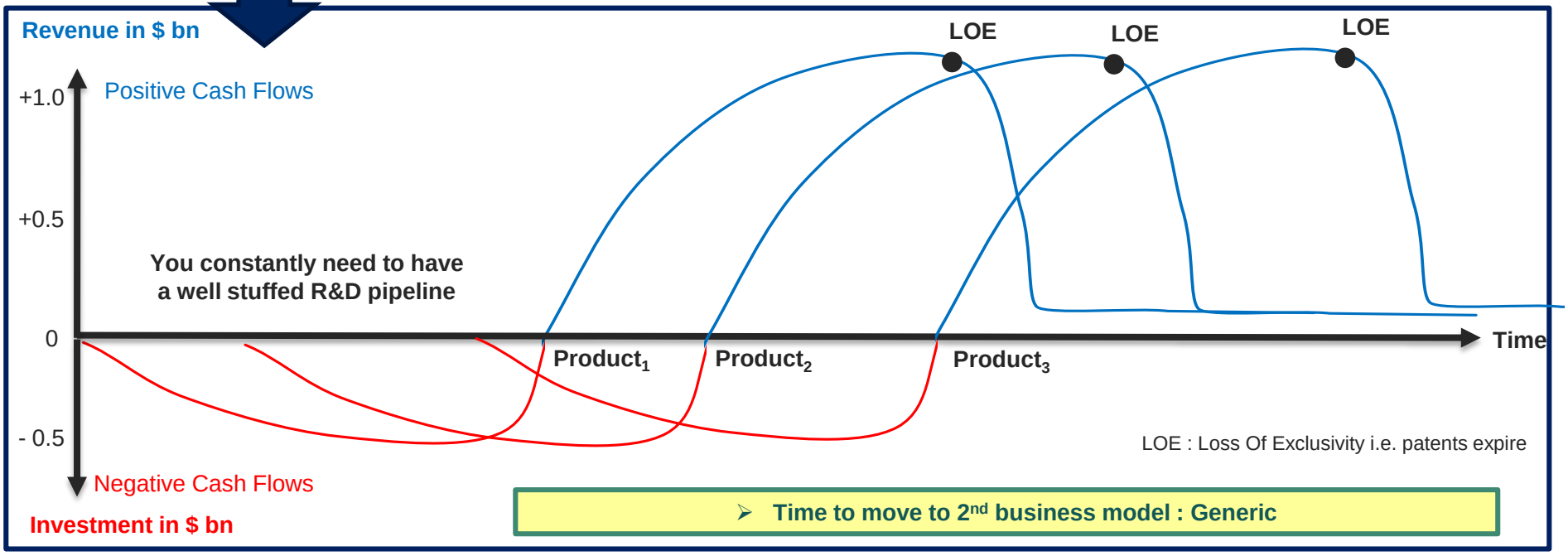
➢ **How do you manage LOE events if you are an innovator ?**

Innovator business model

Pipeline is key

Strategy

- To sustain your sales curve , constantly feed the pipeline
- When you lose exclusivity on a product, ensure you have a new candidate to fill the gap



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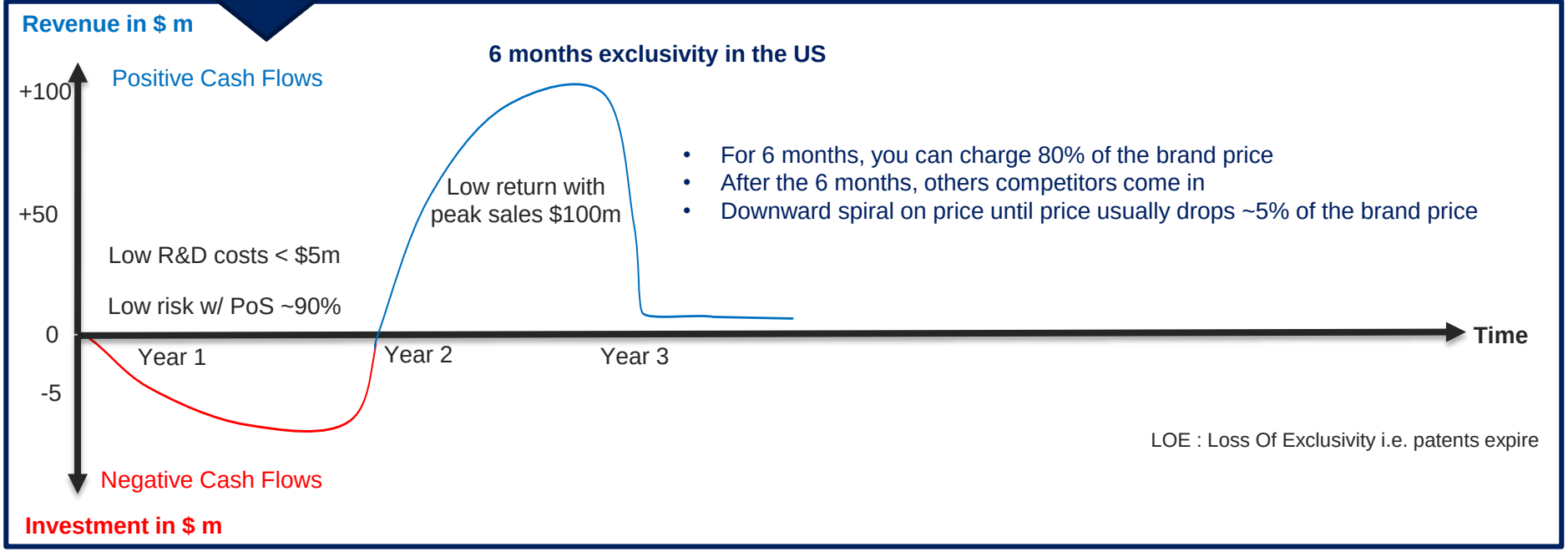
Generic business model

Based on LOE of innovators

Strategy

- Based on LOE of innovators
- Be 1st to market to enjoy 6 months exclusivity in the US (the holy grail of the generic industry)
- Need to constantly refuel pipeline b/c after 6m, sales decrease as a consequence of price competition



- For 6 months, you can charge 80% of the brand price
- After the 6 months, others competitors come in
- Downward spiral on price until price usually drops ~5% of the brand price

LOE : Loss Of Exclusivity i.e. patents expire

Note : curve here is for illustrative purpose only

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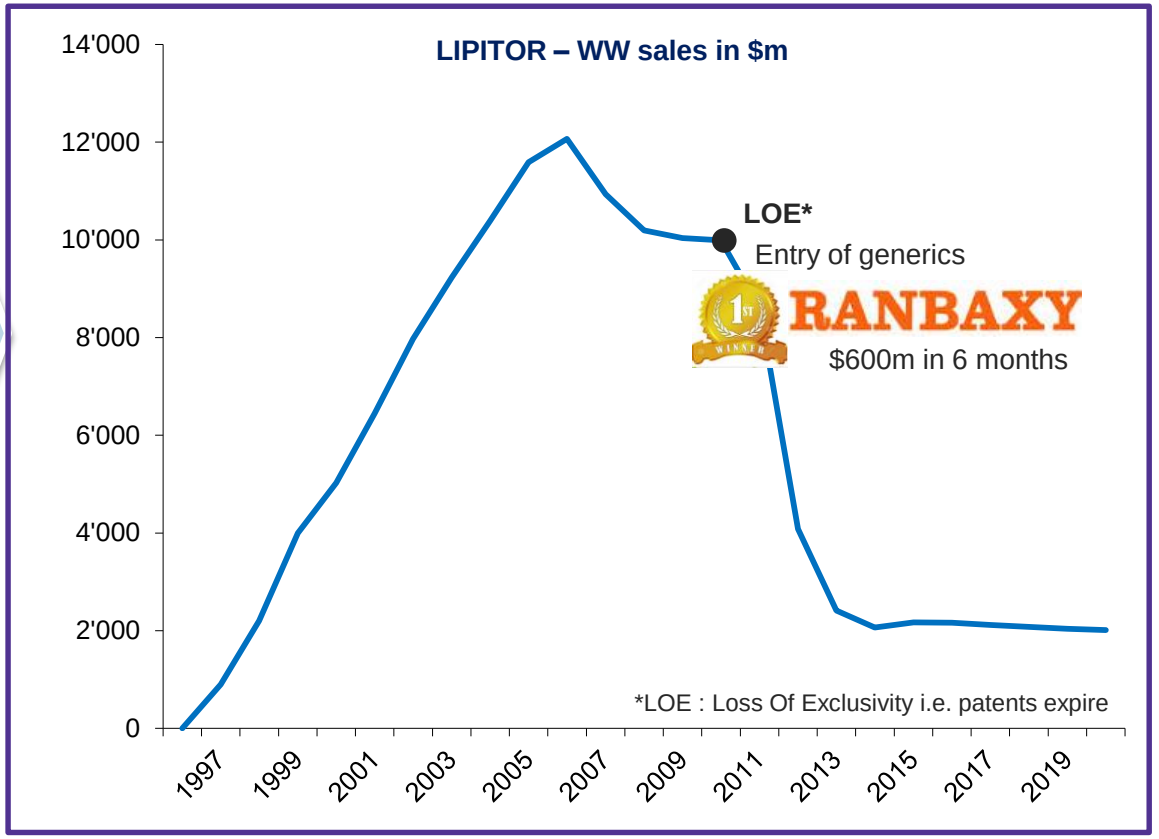
Generic business model

Lipitor case : and the winner is … Ranbaxy

- Ranbaxy : #1 Indian pharma company, 12th-largest WW generics maker
- 2010 sales : $1.9bn
- Generated ~$600 m sales in 6 months



Sources : Evaluate Pharma, http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(11)61858-8/fulltext, http://archive.fortune.com/2011/05/03/news/companies/lipitor_ranbaxy_full_version.fortune/index.htm

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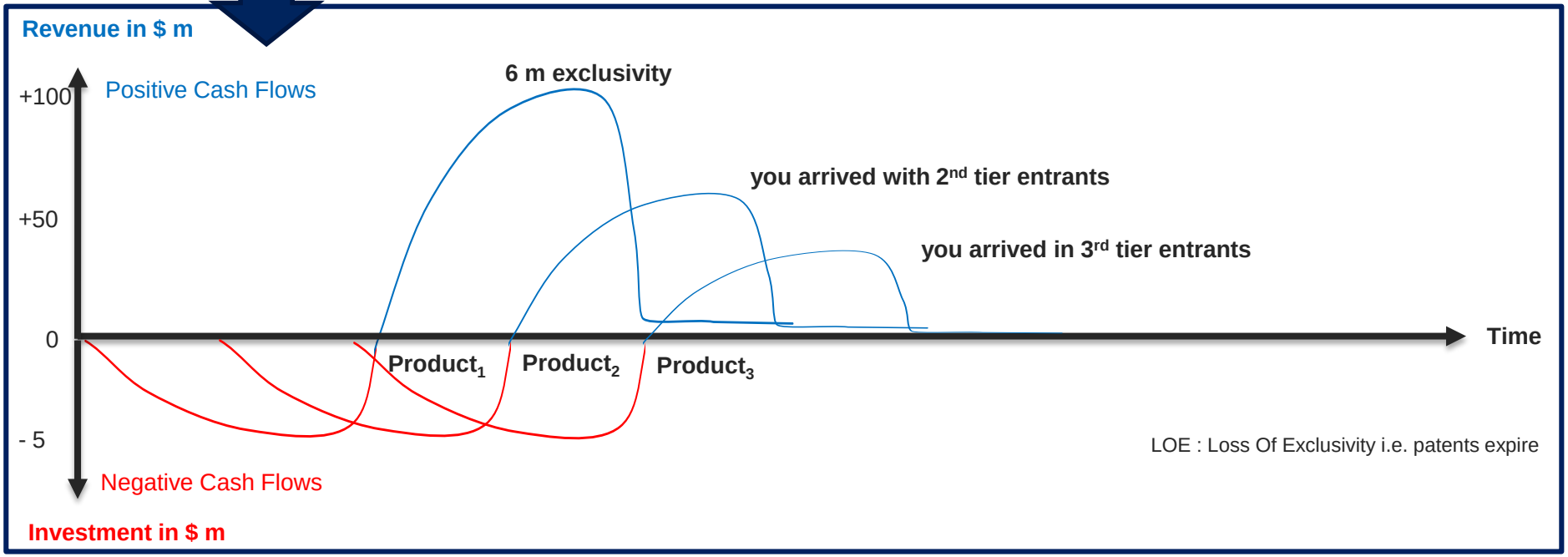
Generic business model
Pipeline is key

Strategy

- Generic business is a mix between **low volume/high price** and **high volume/low price**
- Because you don't always get the 6m exclusivity, and because even if you do it only lasts 6 months, you still need to play in 2nd / 3rd tier, where the strategy is to get a maximum compounds



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OTC business model

Based on product segmentation

Strategy

- Business model closer to FMCG (Fast Moving Consumer Goods)
- Need to reinvent the same product constantly : new formulation, new packaging … new, new, new !
- Hence, pipeline is key

Example : Ibuprofen market

Different brands

Advil

NUROFEN

Anadin

Motrin

NUPRIN

Brufen® 400 Ibuprofenum

Segment patients

by indication, age, drug format

360 solution for your problem

Muscle & Joint pain ?

Source pictures : Google

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OTC business model

Direct-to-consumer marketing is key

Lamisil case

- Brand : Lamisil
- Company : Novartis
- INN : terbinafine
- Launched in 1990s
- Life Cycle Management
  - ✓ Started as Rx pill for onychomycosis
  - ✓ Then expanded indications to athlete's foot & topical forms
  - ✓ After LOE in 2007, launched OTC version
- Built great brand equity with *Digger* as Rx and then leveraged this brand equity in OTC

- **OTC is based on direct-to-consumer marketing**
  - ✓ patient education (e.g. explain onychomycosis)
  - ✓ provide the solution (here Lamisil)

2003 : Digger, the toenail-dwelling mascot

2016 : Digger, the athlete's foot fungus

After LOE, Digger changed careers from onychomycosis to athlete's foot

Source : https://www.youtube.com/watch?v=c4pLm-_YnWs

- Now that you understand the importance of the pipeline, it is time to look at ways to get more compounds

Agenda

1. The pharma business model
2. **How to refuel the pipeline**
3. Prioritize the best compounds within your ideal portfolio

First, the pipeline needs to be balanced between Short Term and Long Term projects

Late stage projects to ensure **short-term business continuity**

Early stage projects to secure **long-term business sustainability**

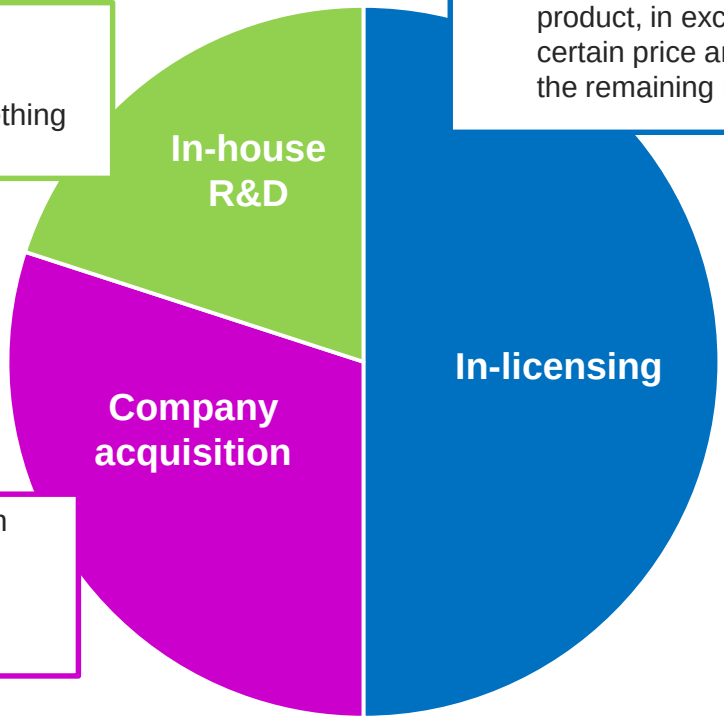
Now that you know what portfolio you want, the next step is to figure out how you are going to get there

How to expand a portfolio with additional candidates ?

3 ways to replenish the pipeline

- This is the cheapest option
- But limited by your resources and discovery yield
- It takes time to do R&D and need luck to find something

- The product is usually still in development
- You buy the rights to commercialize the product, in exchange you have to pay a certain price and royalties, as well as finance the remaining R&D development



- Outright purchase of a company with an existing pipeline
- This is the most expensive option, but available immediately

➢ **80% of big pharma pipeline is sourced externally**

In-licensing

Top 3 selling drugs : all sourced externally

Brand	WW Sales$_{2015}$	Sourced from	Commercialized by		
			US	EU	Japan
HUMIRA adalimumab	$14.4bn	BASF Pharma	abbvie	abbvie	Eisai
Enbrel etanercept	$9.0bn	Immunex	AMGEN	Pfizer	Takeda
Remicade INFLIXIMAB	$8.3bn	Centor	Johnson & Johnson	MERCK	Mitsubishi Tanabe

Sources : annual reports, Evaluate Pharma

What does an in-licensing deal look like?

In-licensing

Case study : Alfa for skin infections – early stage deal

- **Signing fee**
  - $5m
- **Contingent Milestones**
  - Successful Phase 1 : $5m
  - Successful Phase 2 : $10m
  - Successful Phase 3 : $ 30m
  - EMA approval : $15m
  - FDA approval : $ 30m
- **Royalties based on Sales Tranches**
  - 4% on net sales <$100m
  - 8% on $100m< net sales <$250m
  - 12% on net sales >$250m

How far advanced the drug is in development will influence the price paid and the deal structure

Company acquisition

Case study : Roche / Genentech

- Founded in 1896 – based in Switzerland
- 2 divisions : traditional pharma and diagnostics

- In the 1980s, like all established pharma houses, Roche wanted to participate in the genetic engineering revolution
- Roche built its own biologics expertise inside the company, but soon realized others were ahead

➔ To avoid being behind, Roche was looking for a partner that would accelerate its presence in genetically engineered drugs

- Founded in 1973 – based in the USA
- Pioneer in genetic engineering

- IPO in 1980 to raise additional funds to finance R&D
- However, there was a high market volatility for biotech equities resulting in money unexpectedly moving out of biotech and company valuations coming down

➔ When it was unable to interest investors, it started looking for a financial partner in the industry

- Roche entered in an in-licensing/co-promotion agreement with Genentech in 1986
- In 1990, Roche bought 60% of Genentech for $2.1bn
- In 2008, Roche acquired the remaining shares for $ 48bn

➔ The collaboration resulted in some of the top breakthrough drugs of the 20th century

e.g. Rituxan (1997), Herceptin (1998), Avastin (2004), Lucentis (2006)

Sources : Roche 10-k and analyst presentations, Roche website, IMD case : Financial Pioneering: The Genentech Acquisition by Roche by Anna Eckardt

Asset swap

Lisinopril : Merck and ICI*

Background

- Hypertension (ACE inhibitors)
- Dvped by Merck in the early 1990s
- Structure of Deal
  - Merck & ICI both to market the drug WW @ the same time
  - Competing against each other and using different brand names for same therapy
  - In exchange, ICI to give Merck a compound in diabetes with high risk / high potential profile

ICI ZESTRIL LISINOPRIL — **55% market share**

- Needed to boost their lethargic sales
- **Retail** with (1) Smart branding with *Zest*ril - most other Tx for hypertension caused a loss of energy, patients complained that Tx took the *zest* out of lives; and (2) Put entire Pharma division behind Zestril
- **Tender markets** - ICI cut their price. With roots in the bulk chemical trade, where price competition is a way of life, ICI was better at winning tenders - where large buyers were unwilling to pay for the Merck name

⇨ **Better branding, sales force focus and willingness to compete on price**

MERCK PRINIVIL (LISINOPRIL) MSD — **45% market share**

- Prinivil positionned as follow-on therapy to Vasotech
- Merck thought they could beat ICI in marketing Lisinopril – but as Vasotech was booming, marketing teams were less enthusiastic about the 2nd hypertension drug
- Merck was not ready to compete on price
- Merck was very excited about the diabetes compound (which later failed in clinical trials)

⇨ **Overestimated capabilities in research & marketing !**

* : in 1999, ICI (Imperial Chemical Industries Pharma) sold ICI Pharma (Zeneca) to Astra, which then became AstraZeneca

Source : The Moral Corporation: Merck Experiences – by P. Roy Vagelos and Louis Galambos

- Now that you have a full portfolio, you are faced with a new challenge, budget constraints
- As you will not be able to finance all the projects, you have to select the ones that are the best

Agenda

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3. **Prioritize the best compounds within your ideal portfolio**

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Because of limited resources, we have to choose between projects

How to prioritize the projects ?

2017 Budget available only $75m !

	R&D View		Commercial View		To reconcile the different views		2017 R&D costs	
Project	PoS	Ranking	Peak Sales in $m	Ranking	risk adj. NPV in $m	Ranking	Per Project in $m	Cumulative in $m
P-1	95%	#14	80	#12	196	#1	4	4
P-2	33%	#8	320	#1	115	#2	9	14
P-3	77%	#13	134	#10	92	#3	12	26
P-4	100%	#15	55	#14	39	#4	0	26
P-5	53%	#10	98	#11	33	#5	0	27
P-6	53%	#11	41	#15	32	#6	4	31
P-7	62%	#12	159	#7	31	#7	17	48
P-8	47%	#9	215	#4	24	#8	8	56
P-9	9%	#1	267	#2	16	#9	4	60
P-10	15%	#5	192	#5	16	#10	11	70
P-11	19%	#7	140	#9	7	#11	5	75
P-12	9%	#3	220	#3	-1	#12	6	81
P-13	9%	#2	180	#6	-2	#13	9	91
P-14	19%	#6	74	#13	-2	#14	5	96
P-15	9%	#4	148	#8	-6	#15	6	101
Drivers	NCE over LCM		Peak Sales, Launch date		Timing, Risk, Cost, Sales			

Discontinue below the red line

PoS : Probability of Success

NPV : Net Present Value

Priority

High | Medium | Low

Note : numbers for illustrative purposes only

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The NPV measure is the golden standard to rank projects, hence it is important to understand how it works

- Brief overview of NPV
- The concept of NPV and risk-adjusted NPV

NPV : Net Present Value

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Overview of the NPV measure

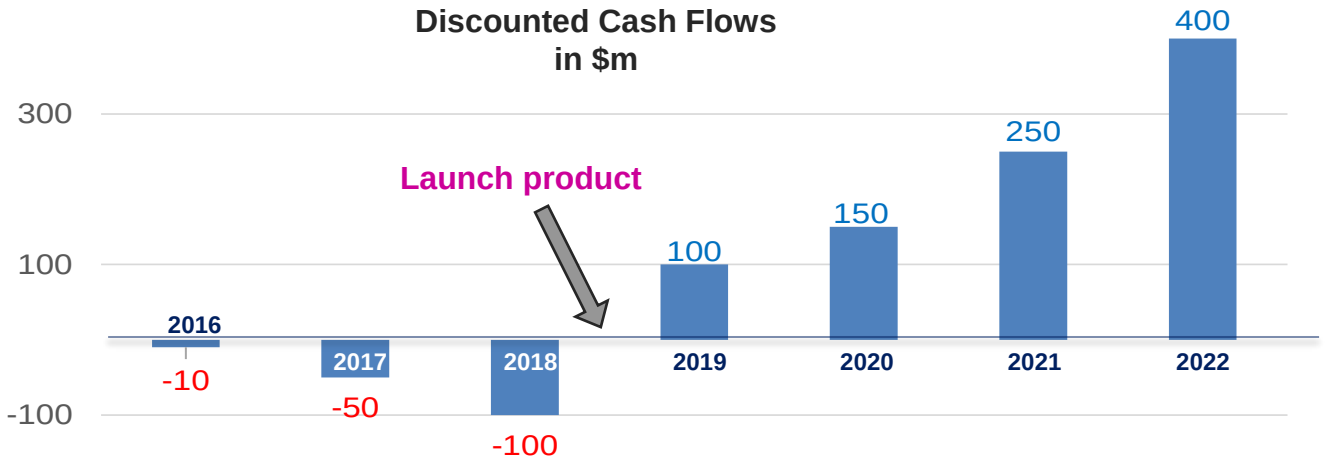
What is the NPV ?

The NPV is the value of the project today
It is calculated as the sum of the Discounted Cash Flows

What are Discounted Cash Flows ?

Discounted Cash Flow = Revenue – Costs – R&D investment – Cost of capital

Example



NPV = -10 -50 -100 +100 + 150 +250 +400 **= $740m**

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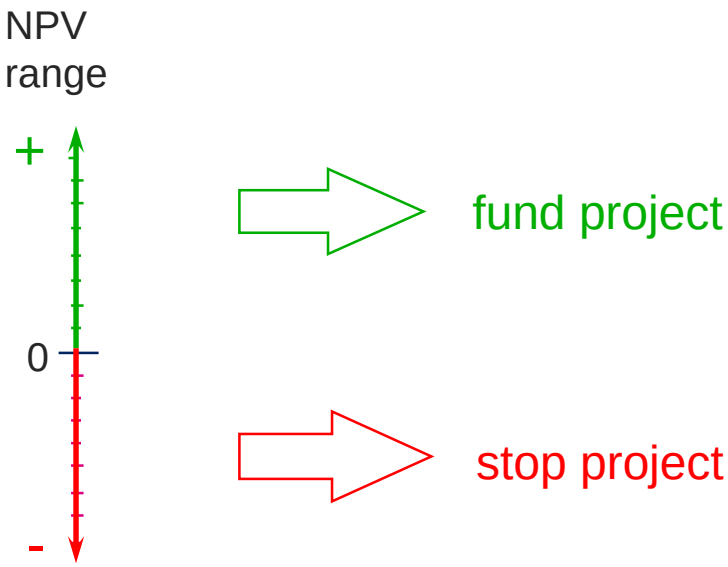
Valuation Principles

The NPV Analysis leads therefore to a simple decision rule



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What is specific to R&D projects ?

In the case of R&D projects you also need to take risk into account

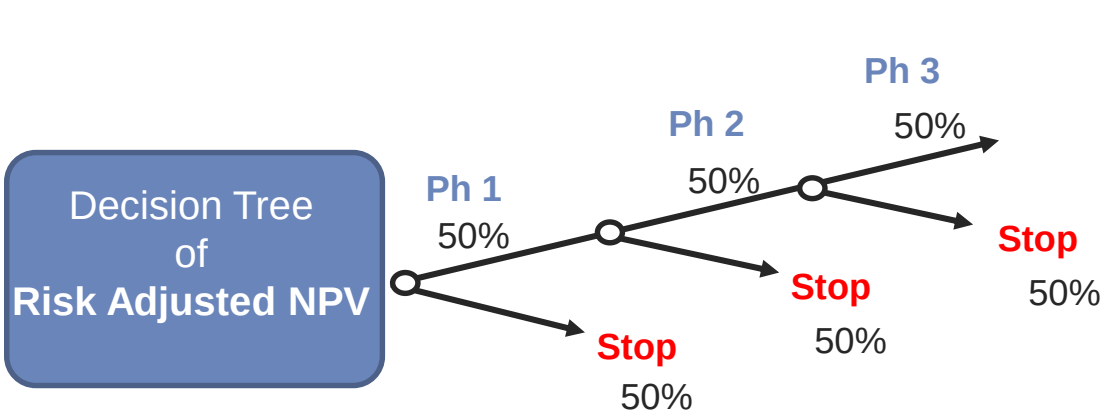
How ?

By adjusting cash flows using a risk factor

How ?

Valuation Principles

The decision tree of risk adjusted NPV



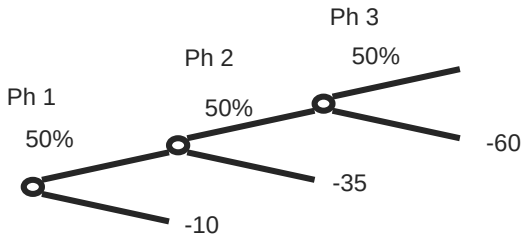
Let's look at an example

Valuation Principles

Adjusting for risk through cash flow calculation

Example Product in Phase 1

Risk Adjusted NPV



Risk adjusted NPV is significantly less than the NPV because we have rightly adjusted for the risk in the project

	2016	2017	2018	2019	2020	2021	2022
	Ph 1	Ph 2	Ph 3	On the market			
Probability of success	50%	50%	50%				
Probability of spending	100%	50%	25%	12.5%			
Discounted Cash Flows	-10	-50	-100	100	150	250	400
						=> NPV	740

Risk adjusted	= 100% x -$10m	= 50% x -$50m	= 25% x -$100m	= 12.5% x $100m	= 12.5% x $150m	= 12.5% x $250m	= 12.5% x $400m
Discounted Cash Flows	-10	-25	-25	13	19	31	50
						=> risk adj. NPV	53

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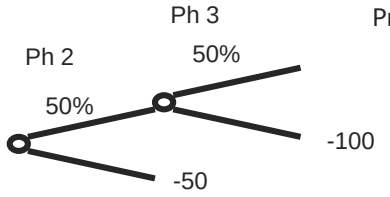
Valuation Principles

Adjusting for risk through cash flow calculation and moving ahead in time

Same Product – Now in Phase 2

Risk Adjusted NPV



NPV only includes costs going forward

i.e. past costs (a.k.a. sunk costs) are not included in the valuation

	2017	2018	2019	2020	2021	2022
	Ph 2	Ph 3	On the market			
Probability of success	50%	50%				
Probability of spending	100%	50%	25%			
Discounted Cash Flows	-50	-100	100	150	250	400
					=> NPV	750
						+10 vs if in Ph 1

Risk adjusted	= 100% x -$50m	= 50% x -$100m	= 25% x $100m	= 25% x $150m	= 25% x $250m	= 25% x $400m
Discounted Cash Flows	-50	-50	25	38	63	100
					=> risk adj. NPV	125
						+72 vs if in Ph 1

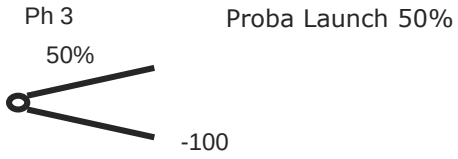
Higher valuation of the same project as time advances …

Valuation Principles

Adjusting for risk through cash flow calculation and moving **further** ahead in time

Same Product – Now in Phase 3

Risk Adjusted NPV



		2018	2019	2020	2021	2022
		Ph 3	On the market			
Probability of success		50%				
Probability of spending		100%	50%			
Discounted Cash Flows		-100	100	150	250	400
					=> NPV	800
						+60 vs if in Ph 1

Risk adjusted		= 100% x -$100m	= 50% x $100m	= 50% x $150m	= 50% x $250m	= 50% x $400m
Discounted Cash Flows		-100	50	75	125	200
					=> risk adj. NPV	350
						+297 vs if in Ph 1

Because of its mathematical properties, risk-adjusted NPV gives a higher valuation to late stage projects due to lower risk and shorter time to market

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Is it possible to work with NPV only ?

What is missing in the NPV ?

Need to balance the portfolio between early stage and late stage project	Commercial risk	Strategic Fit
▶ Risk-adjusted NPV gives a higher valuation to late stage projects ▶ Wrongly skewing the decision towards late-stage projects ▶ Risk of unbalanced portfolio	▶ NPV is based on sales forecasts but it does not tell you how easy it would be to reach or not these forecasts	▶ NPV does not tell you how important the project is for the company's strategy

Complementary measures exist, but NPV stays the Golden Standard

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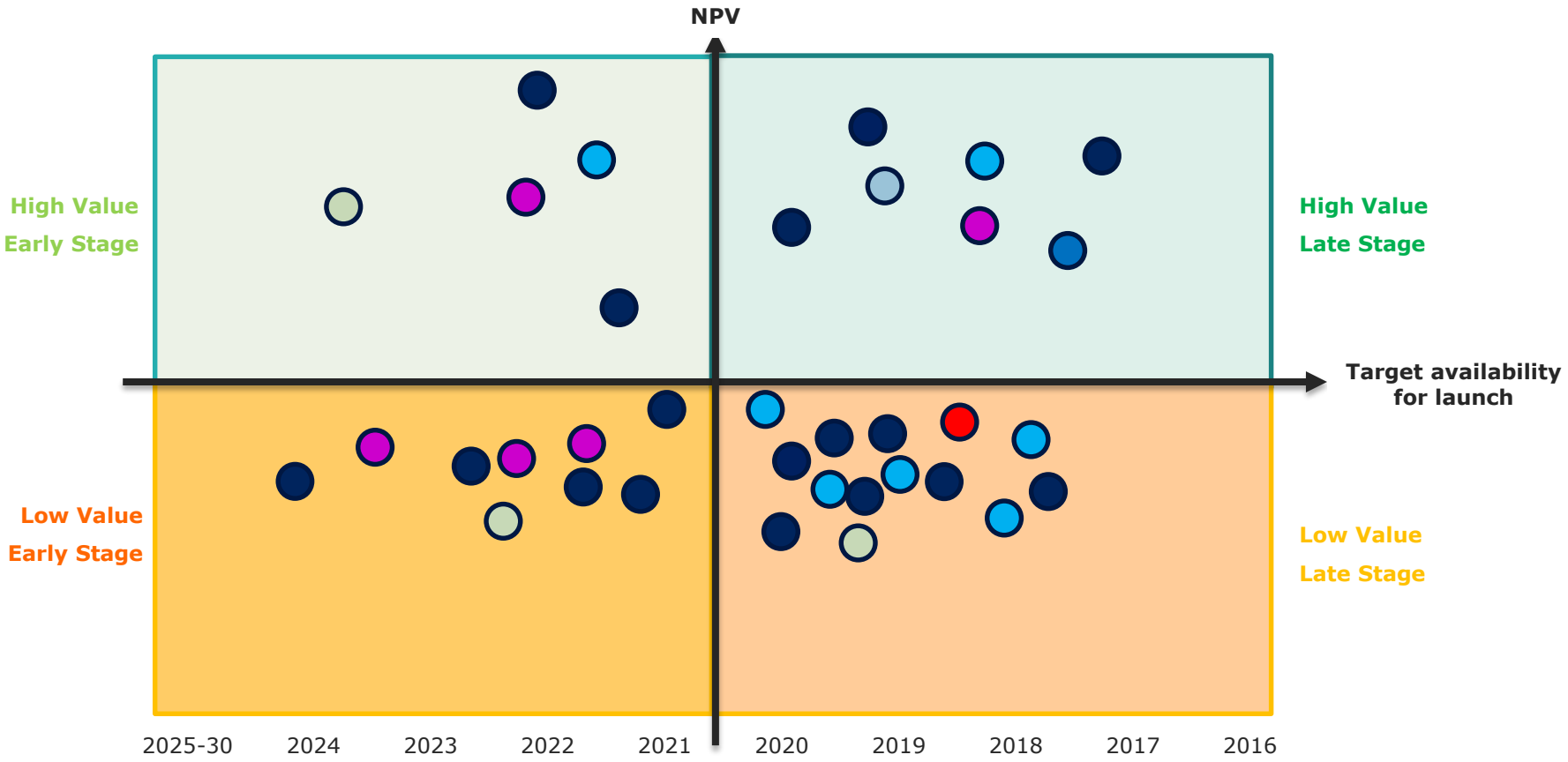
Portfolio optimization : focused selection

"The essence of strategy is choosing what not to do", Michael Porter



Note : graph here is for illustrative purpose only

Adapted from Effective Porfolio Management, Ewa Krol, 14th Annual Strategic Project & Porfolio Management for Pharma Congress, Barcelona, 2015

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Key take-aways

- **3 major business models : Innovator, Generic, OTC**
- **3 ways to refuel a pipeline : In-House, In-Licensing, Company Acquisition**
- **The Net Present Value (NPV) measure is the golden standard used to prioritize compounds in a portfolio**
- **A well-balanced portfolio between short term projects and long-term projects is key for a healthy business**
- **Portfolio selection is a product of cross-functional analysis that results in a decision matrix where risk and reward are balanced and the final selection of candidates is also function of the budget available**