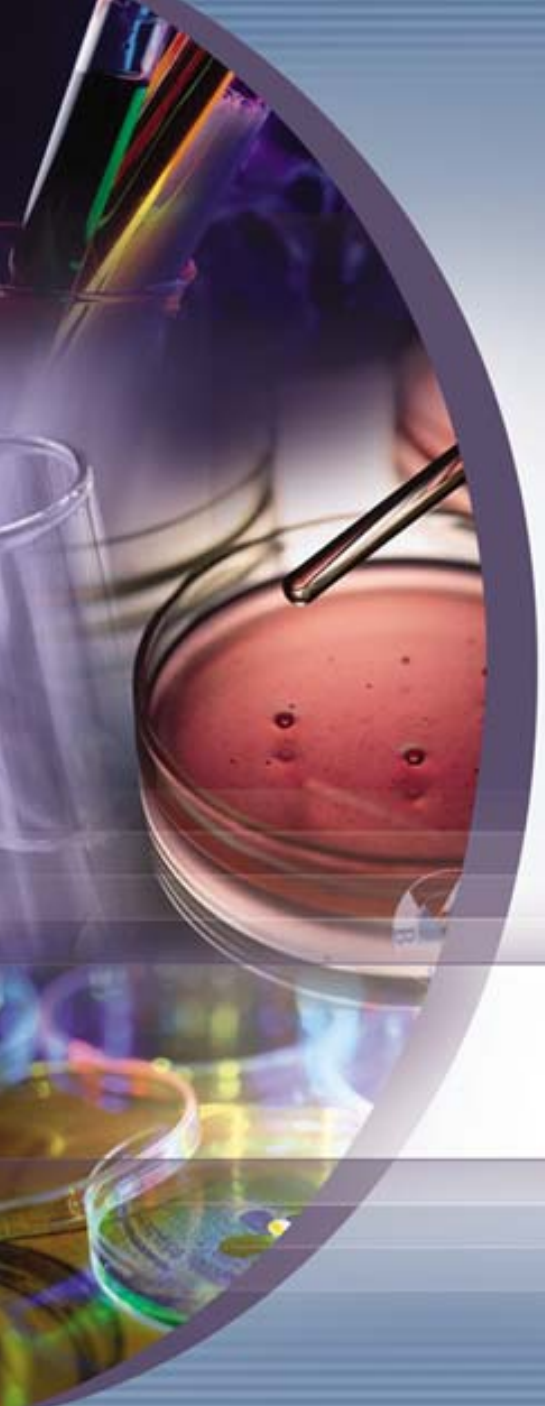


X-biotech

Ecole des Mines

24 April 2006

novexel
novel therapies for infectious disease

Agenda

- Pharmaceutical Industry Context
- Antibiotic Therapeutic Area
- Creation and Structure of Novexel SA
- Pipeline Attributes
- 2006 Milestones

Bigger is Better ?

1992
Industry Sales : $ 226 Billion

	Market Share (%)
Merck & Co	3.9
Glaxo	3.7
BMS	3.3
Ciba-Geigy	2.8
SKB	2.7
Hoechst	2.5
J&J	2.5
AHP	2.4
Pfizer	2.3
Bayer	2.2
Top 10	**28.3**

2004
Industry Sales : $ 550 Billion

	Market Share (%)
Pfizer	9.3
GSK	6.0
sanofi-aventis	5.0
J&J	4.5
Merck	4.3
Novartis	4.2
AZ	3.9
Roche	3.2
BMS	2.8
Wyeth	2.6
Top 10	**45.8**

Source : IMS

Growth through M&A

Kabi Pharmacia

+

1993 - Farmitalia CarloErba

1995 - Upjohn

1999 - Sugen

2000 - Searle Monsanto

PHARMACIA

+

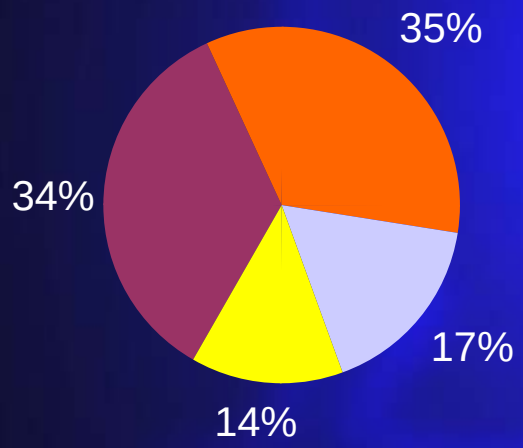
Pfizer

	1992	2001	2003
Ranking	*#41*	*#9*	*#1*
% Share	*0.6*	*3.2*	*10.5*

Role of USA

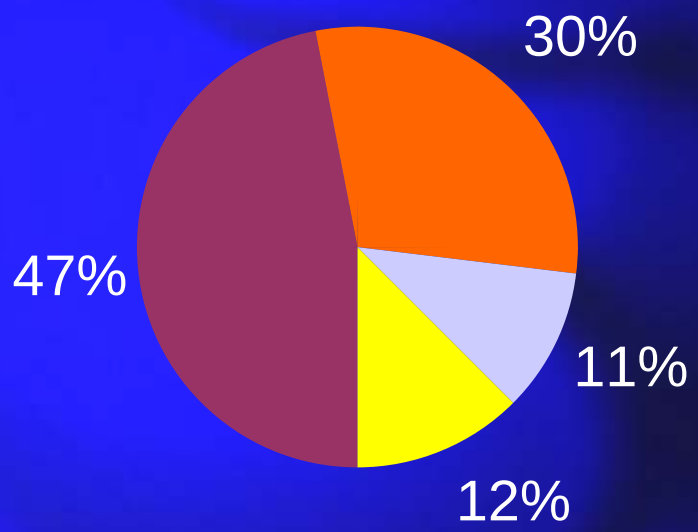
1992

$ 218 Billion



2005

$ 566 Billion



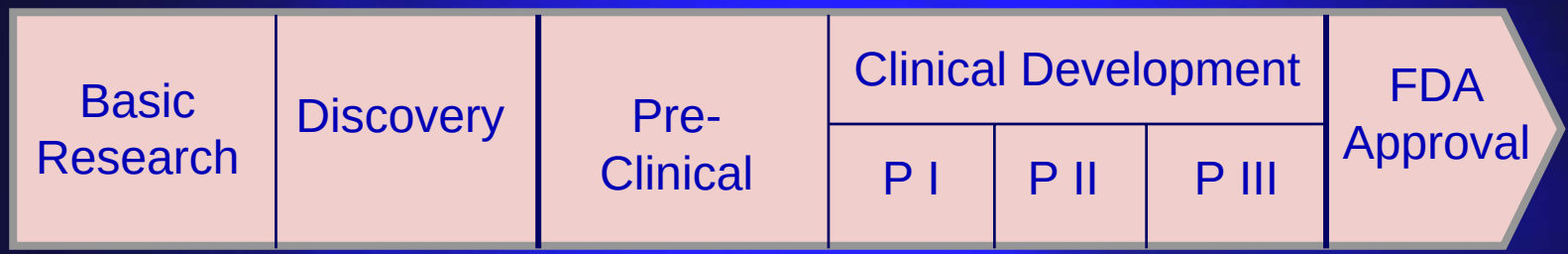
North America **Europe** **Japan** **Other**

Source : IMS

The R&D Process

"…One third of molecules now in development originated in biotech companies…"

Source : The Economist - Pharmaceutical Survey June 2005



Years	2.5	3.0	1.0	1.5	2.0	2.5	1.5	14.0
Cost (%)	4%	15%	10%	15%	22%	31%	3%	100%

6.0
78%

Source : McKinsey & Co, Lehman Brothers, PhRMA, FDA

Generic Erosion

"…Over the next 5 years, a record 70 billion-worth of drugs will face generic competition in America alone…"

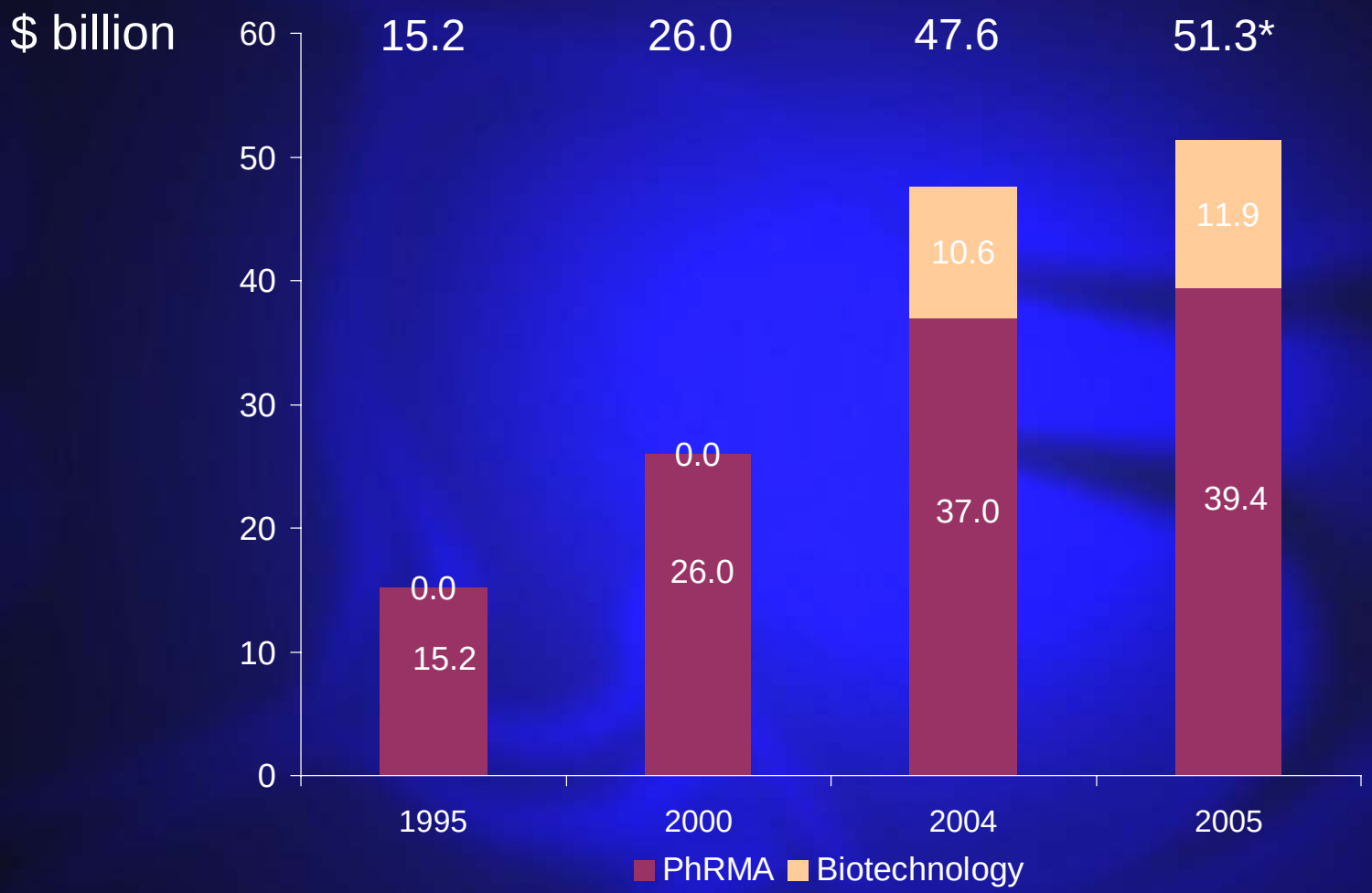
Source : The Economist - Pharmaceutical Survey June 2005

Diflucan® Drop : Impact of Generic fluconazole…….

	2005	2004	+/- %
USA	(17)	417	***
International	515	528	(2)
Total	498	945	(47)

Source : Pfizer Company Reports

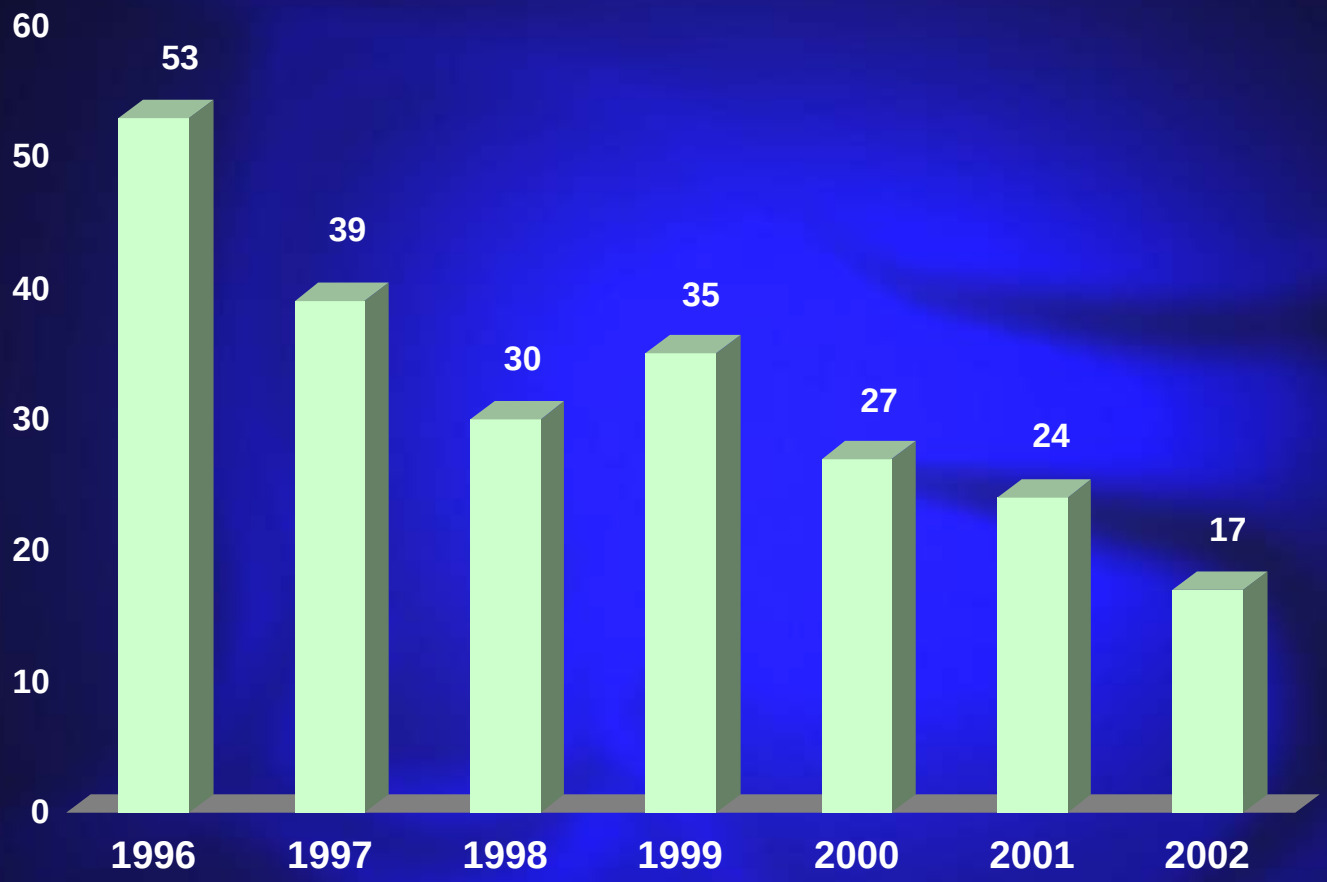
Source of Innovation ?



Source : PhRMA Annual Report

** Estimate*

NME Approvals by FDA



Source : FDA Center for Drug Evaluation & Research - 2002

Megatrends

- Consolidation
  - Pipeline access through M&A
  - Seek Financial Efficiencies
- USA-centric market
  - But co-payment resistance
  - Greater government role
  - But…Role of Emerging Markets (India and China)
- Regulatory Demands
  - Large Safety Databases
  - Post-marketing Surveillance
- Pipelines Pressures
  - Increased Complexity And Price of Innovation
  - More Outsourced R&D
  - Competition for Late Stage Assets (pricing)
  - Generic Erosion / High Profile Withdrawals

Margin Pressure ?

Need to access innovative pipeline

Existing portfolio under threat

Form “biotech” alliances

Further erosion of margins

Agenda

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Antibiotic R&D Exits ?

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novel therapies for infectious disease

Company	*Exit ?*	*Spin Off*	*Divested Assets*
Pfizer	No		
GSK	No		
sanofi-aventis	Yes	Novexel	
Johnson & Johnson	No		
Merck	No		
Novartis	Yes	Nabriva	
AstraZeneca	No		
Roche	Yes	Basilea / Arpida	
Bristol-Myers Squibb	Yes		
Wyeth	No		
Abbott Labs	Yes		cethromycin
Eli-Lilly	Yes		daptomycin
Schering Plough	No		garenoxacin
Bayer	Yes	Hexal Family	

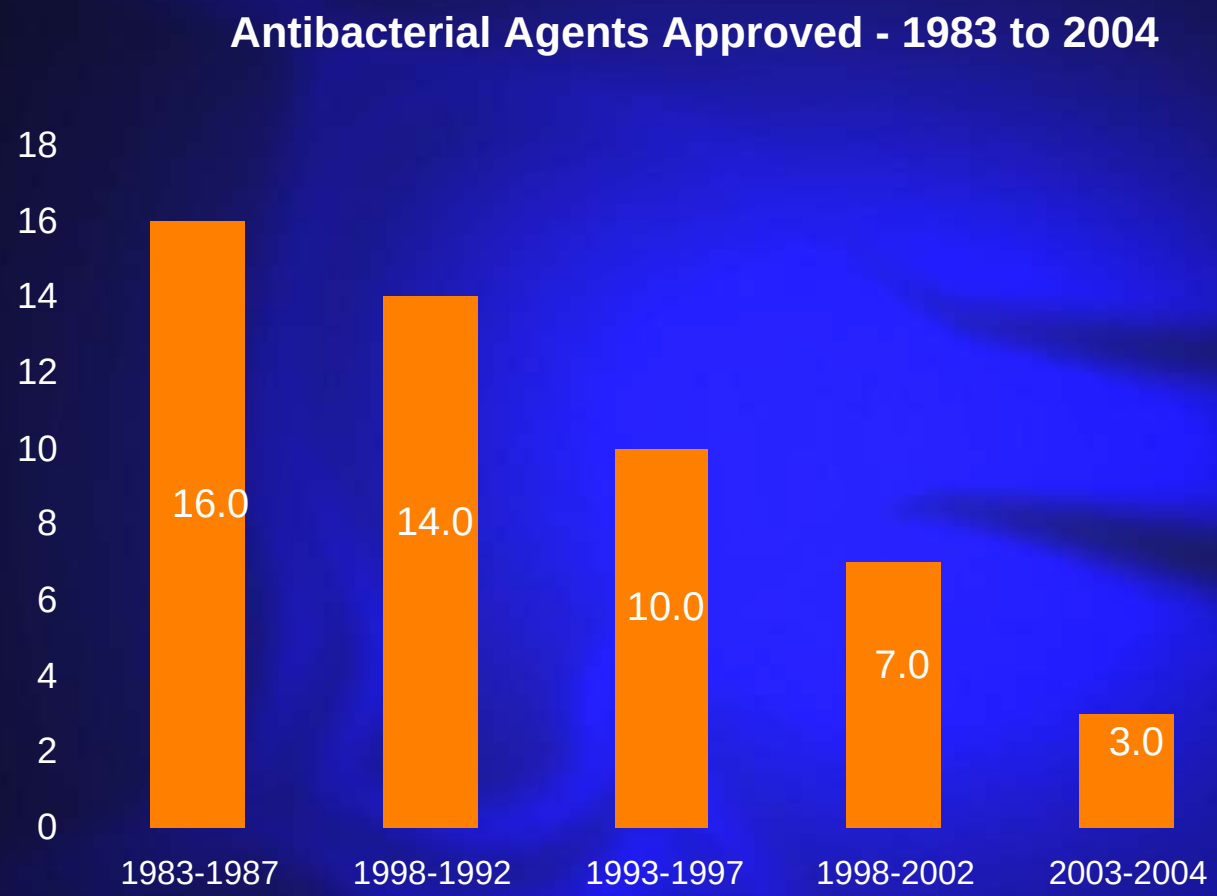
Reasons for Leaving

- Less attractive market
  - Slow overall growth
  - Generic erosion
  - Acute vs Chronic therapy
- Portfolio Optimisation
  - Comparative NPV
  - Focus on antivirals as anti-infectives
- Poor success of novel discovery
  - Genomic Approaches
  - Difficulty to find conserved targets
- Increased Regulatory Demands
  - Safety
  - Statistical requirements to prove superiority

Source : Why is big Pharma getting out of antibacterial drug discovery ?

*- S.J. Projan - Curent Opinion in Microbiology 2003, **6** 427-430*

Reduced Output



Source : Spellberg et al Clinical Infectious Diseases, May 2004

Late Stage Assets

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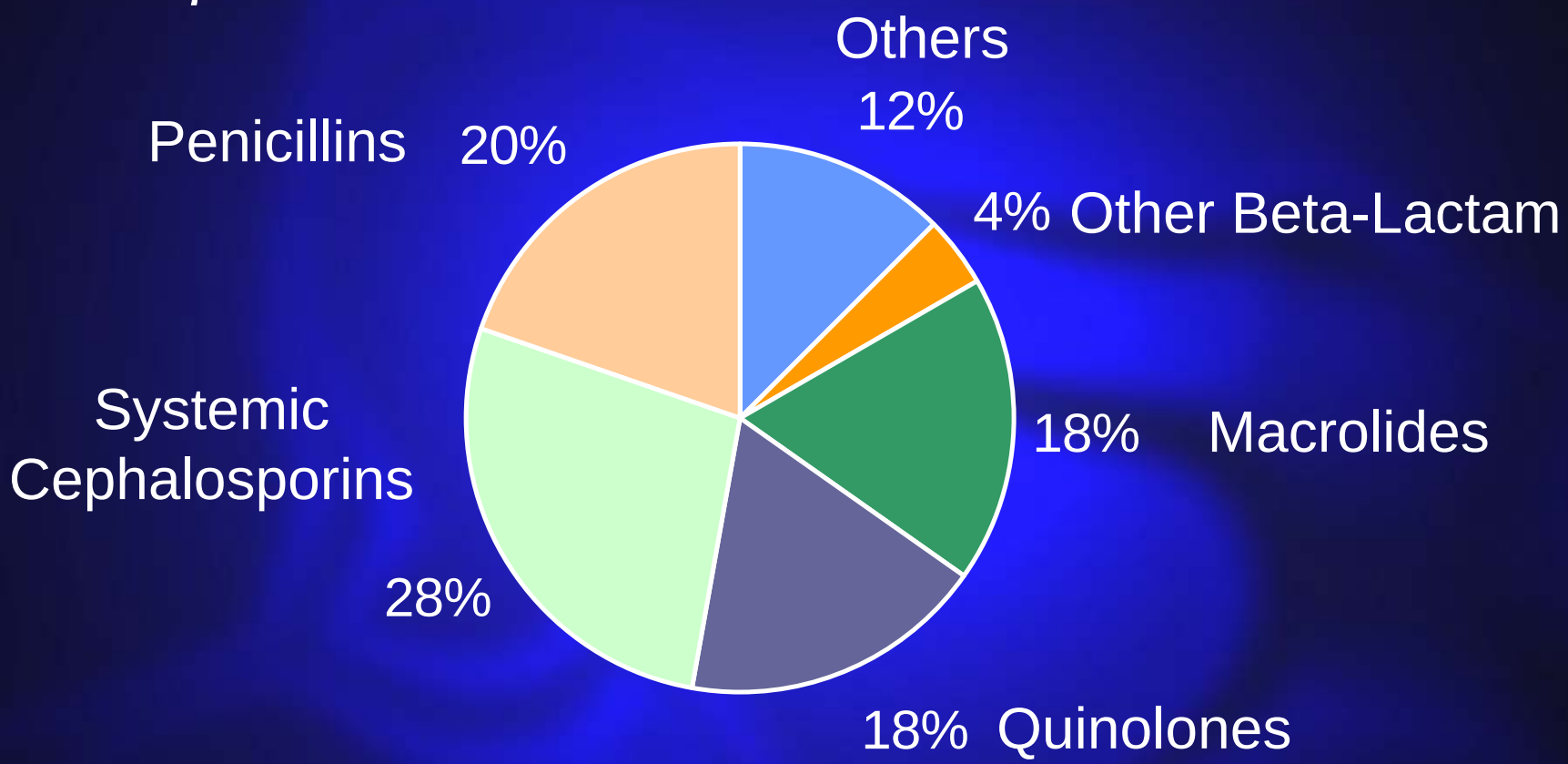
Company	*Headquarters*	*Lead Compound*	*Phase*
Cubist	USA	daptomycin	Market
Oscient	USA	gemifloxacin	Market
Viropharma	USA	Vancocin	Market
Vicuron (Pfizer)	USA	dalbavancin	Filed
Advanced Life	USA	cethromycin	Phase III
Optimer	USA	Prulifloxacin	Phase III
Basilea	Switzerland	ceftobiprole	Phase III
Peninsula (J&J)	USA	doripenem	Phase III
Arpida	Switzerland	iclaprim	Phase III
Theravance	USA	telavancin	Phase III
Replidyne	USA	faropenem	Phase III

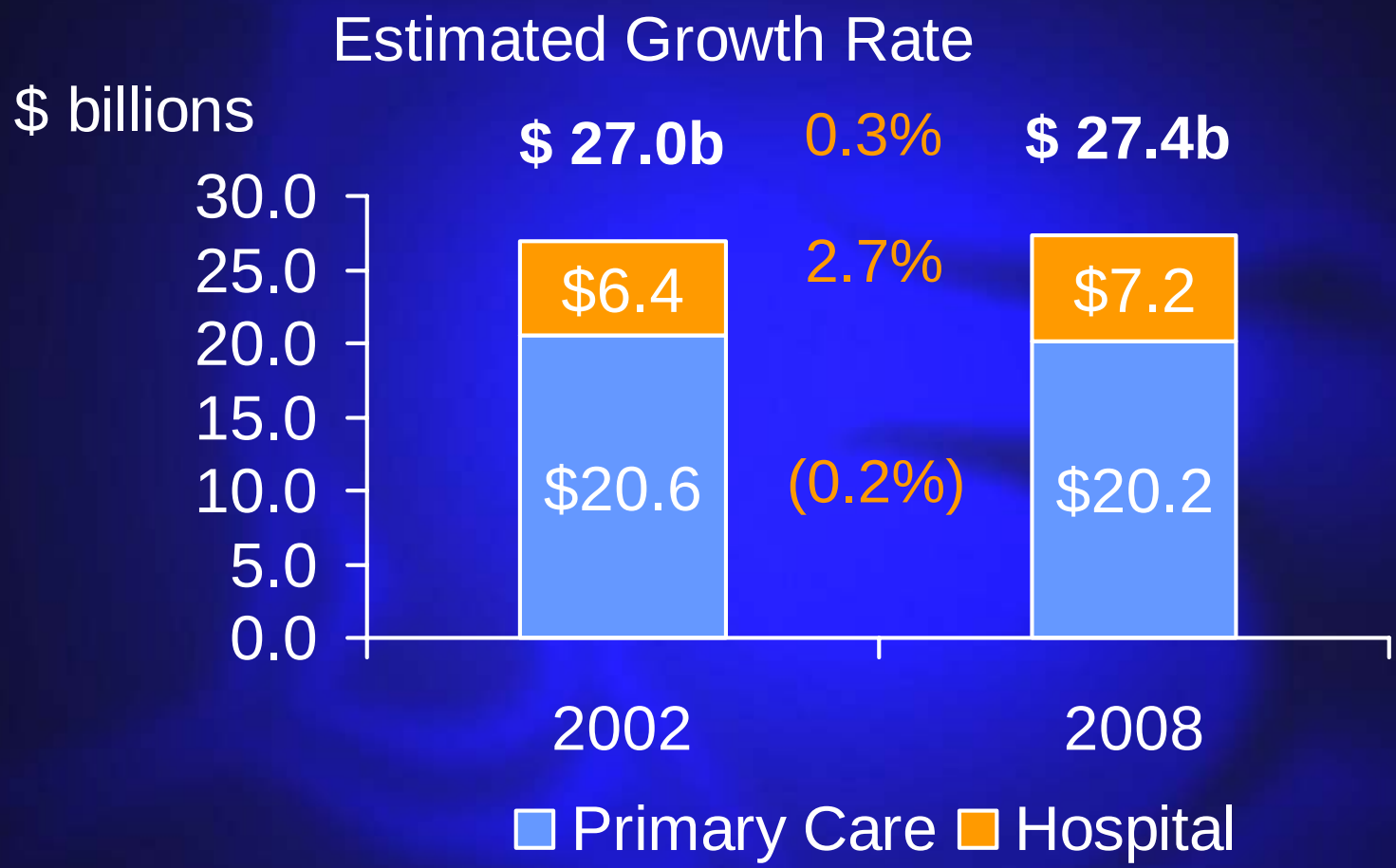
Antibiotic Market - 2004

>50% = β Lactam Class



Source : IMS Reports

Antibiotic Market



Source : Datamonitor Reports

Hospital Brands ($m)

novexel
novel therapies for infectious disease

Name	Compound	Company	2003	2004	2005
Rocephin	ceftriaxone	Roche	1,085	1,004	713
Zosyn	pip/tazo	Wyeth	639	760	892
Primaxin	Imipen /cilastin	Merck	630	641	740
Zyvox	linezolid	Pfizer	181	463	618
Merrem	meropenem	A Z	346	423	505
Maxipime	cefipime	Elan	109	118	140
Invanz	ertapenem	Merck	37	63	94
Cubicin	daptomycin	Cubist	2	59	114
Total			1,944	2,527	3,103
+/-				*30%*	*23%*

Source : company reports

True Novelty ?

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novel therapies for infectious disease

Antibacterial	*Year*	*Novelty*
rifapentine	1998	No
Synercid	1999	No
moxifloxacin	1999	No
gatifloxacin	1999	No
linezolid	**2000**	**Yes**
cefditoren pivoxil	2001	No
ertapenem	2001	No
gemifloxacin	2003	No
daptomycin	**2003**	**Yes**
telithromycin	2004	No

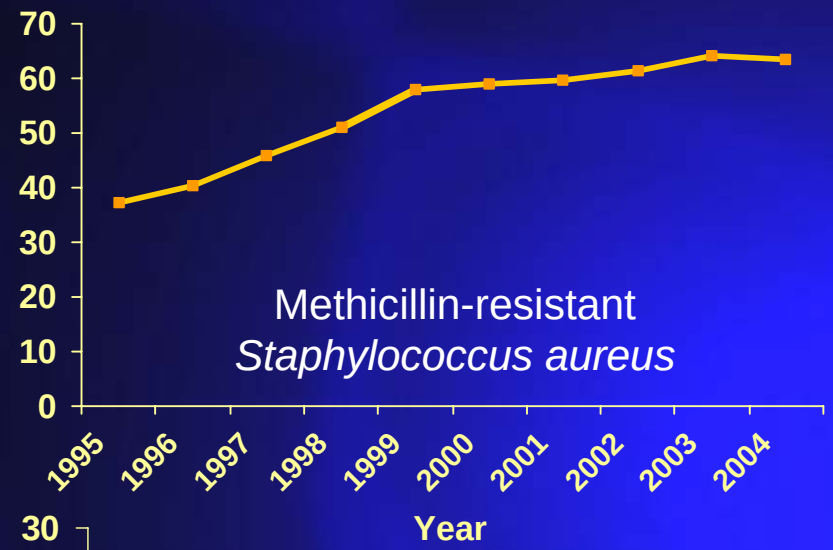
Source : Spellberg et al Clinical Infectious Diseases, May 2004

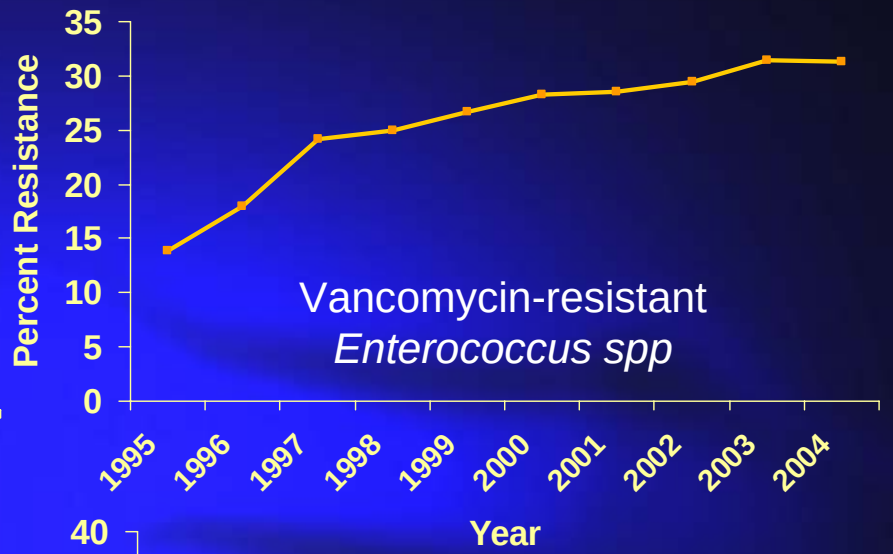
Resistance

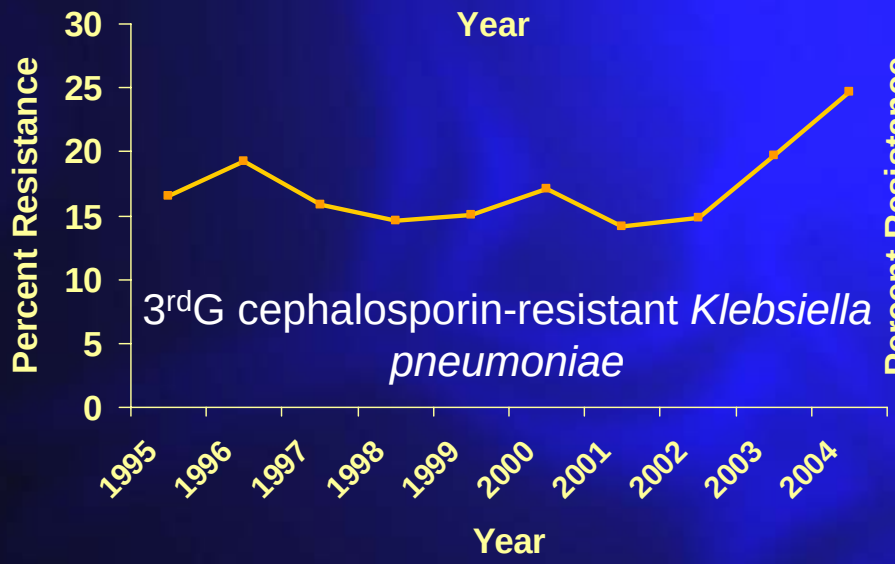
Pathogen	Resistance	%	Estimated # Cases
S. aureus	methicillin	57.1	102,000
enterococci	vancomycin	27.5	26,000
P. aeruginosa	Quniolone	32.8	
*CNS**	methicillin	89.1	130,000
E.coli	ceftazidime	6.3	
K.pneumonia	ceftazidime	14.0	11,000
P. aeruginosa	imipenem	22.3	16,000
P. aeruginosa	ceftazidime	30.2	12,000
Enterobacter spp.	ceftazidime	32.2	
S. pneumoniae	penicillin	11.3	

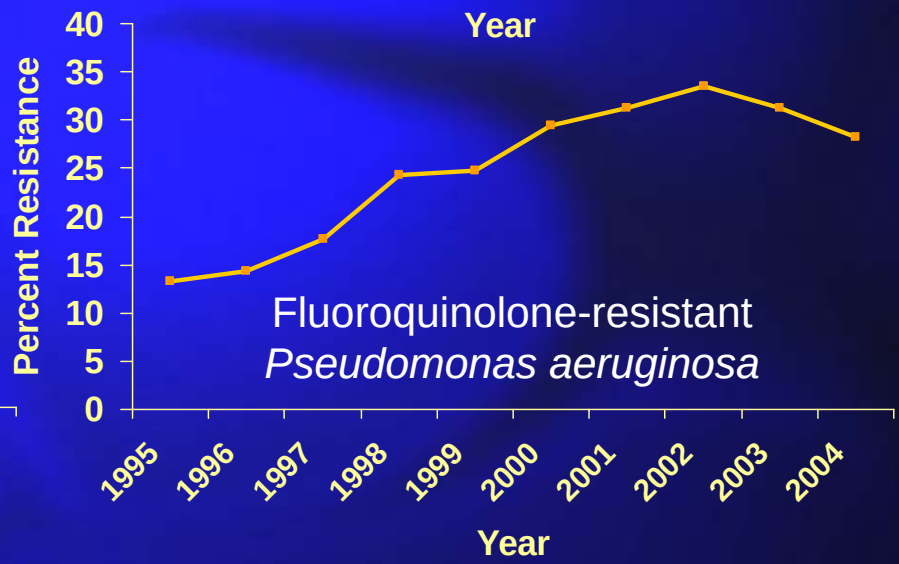
Source: Centers for Disease Control
** Coagulase-negative staphylococci*

ICU Antibiotic Resistance









Source : National Nosocomial Infections Surveillance (NNIS) System Report October 2004

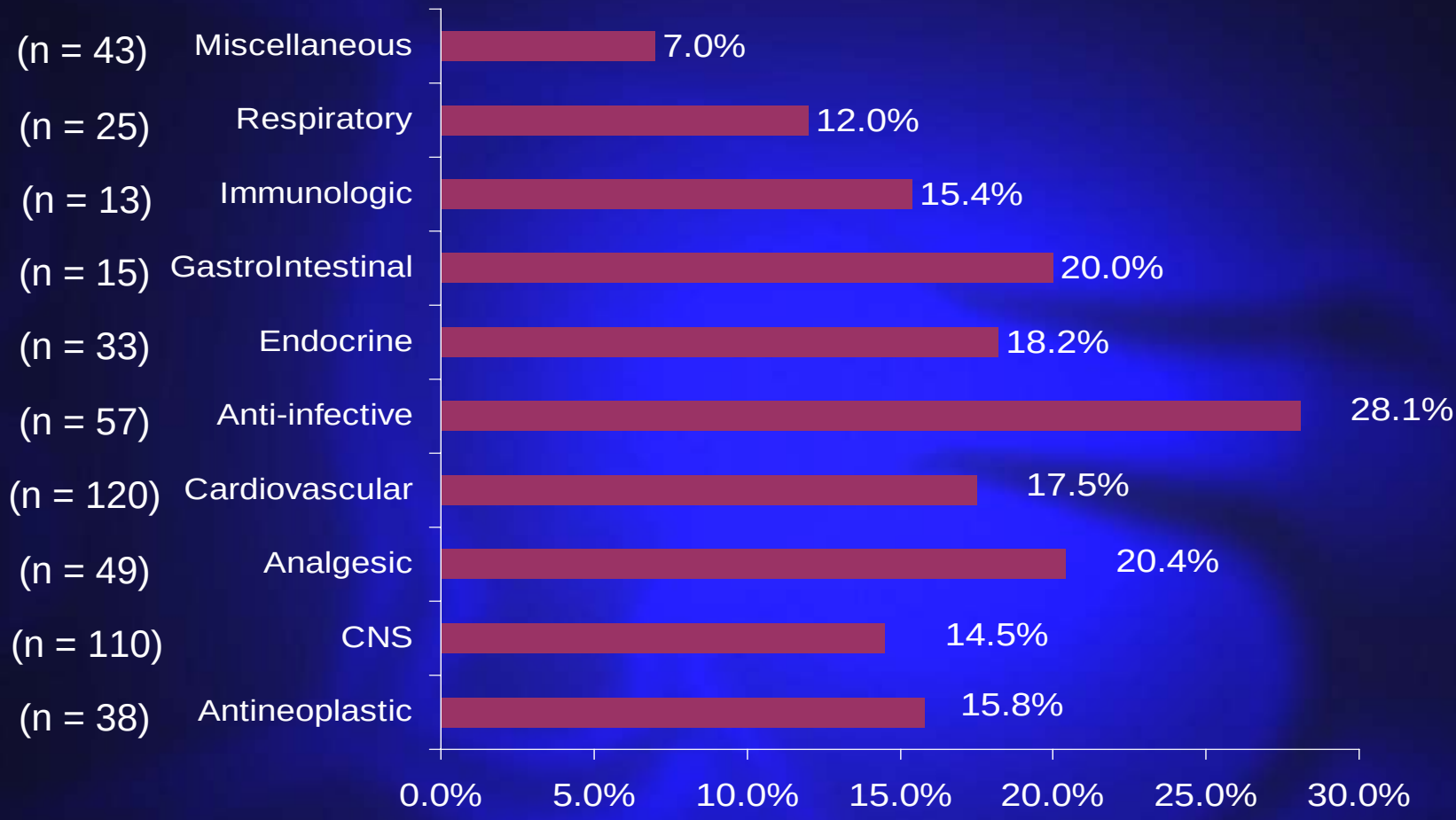
Unmet Need

Hospital Infections

- Activity against resistant pathogens
- Shorter treatment courses
- Oral / i.v. switch capacity
- Cost
- Improved side effect profile

Source : Datamonitor Report Antibacterials - December 2003

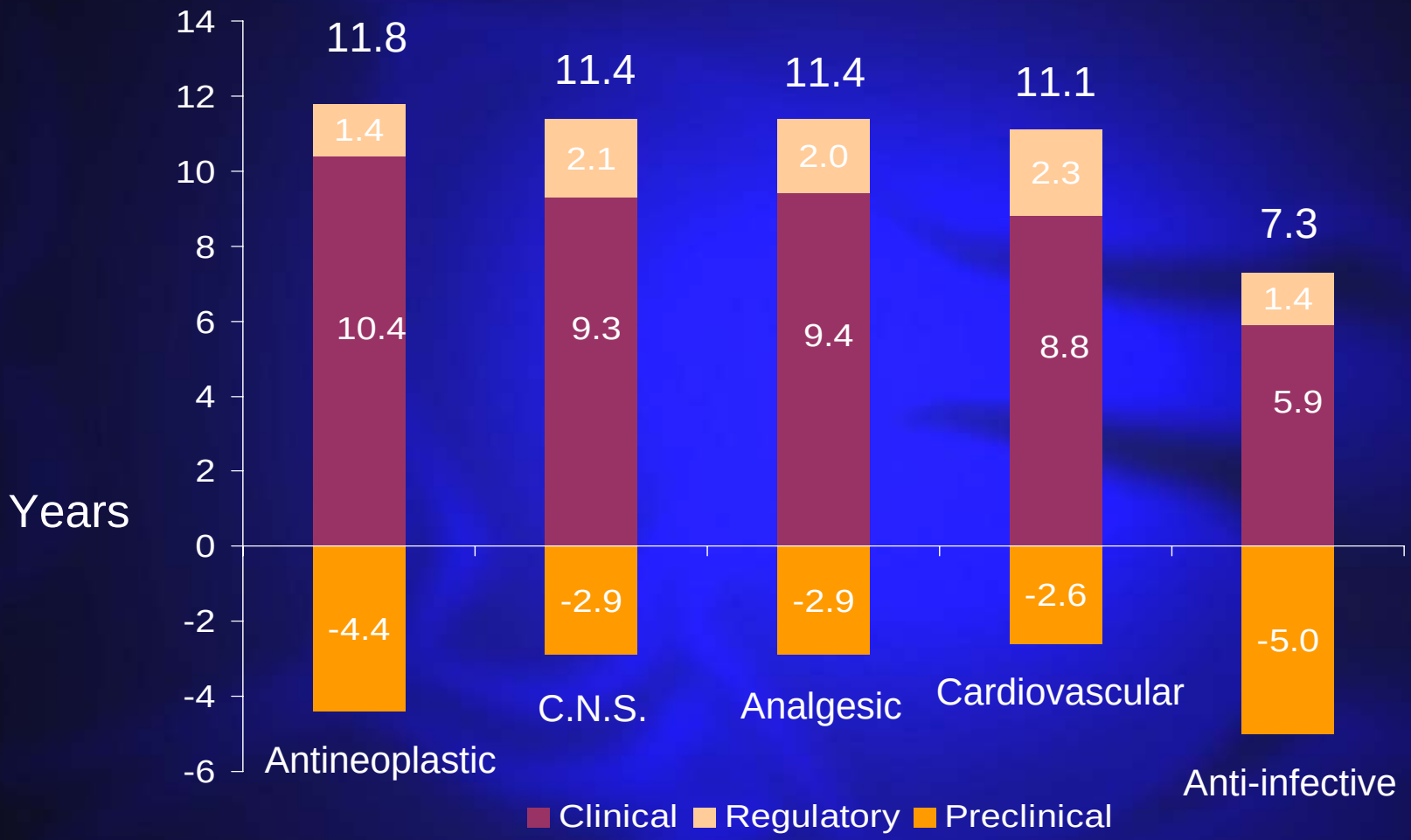
NCE Success* Rate



* Note : Success = IND Filing (1981-1992) to NDA Approval at December 1999

Source : J. A. DiMasi – Tufts – Database Clinical Pharmacology & Therapeutics 69, Number 5

NCE Development Time



Source : J. A. DiMasi – Clinical Pharmacology & Therapeutics 69, Number 5

Anti-infective Deals 2005

novexel
novel therapies for infectious disease

Company	*Partner*	*Compound*	*Transaction Date / Amount*
J&J	Basilea	ceftobiprole	License February 2005 CHF370m
J&J	Peninsula	doripenem	Acquisition June 2005 $245m
Pfizer	Vicuron	anidulafungin dalbavancin	Acquisition June 2005 $1,900m
Astellas	Theravance	telavancin	License November 2005 $221m

The Opportunity

- Examples of large pharmaceutical companies who have abandoned anti-infective R&D but renewed appetite by certain players
- Resultant fragmentation of sector
- Growing need for new agents to combat increasing threat and incidence of resistant strains
- Hospital segment of recent introductions is >$3 b and growing rapidly
- Hospital based sales effort will not require large commercial infrastructure

Agenda

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Romainville History

1920	"L'institut de Serotherapie Haemopoietique" (ISH) founded by Dr Gaston Roussel around "Hemostyl"
1928	Creation of "Usines Chimiques des Laboratoires Francais" (UCLAF)
1940s	Jean-Claude Roussel and creation of "Sofrapen" (Societe Francaise de la Penicilline) Creation of Roussel-Uclaf
1961	Hoechst – Majority Shareholder
1980	Launch of Claforan (cefotaxime or HR756)
1997	Hoechst Marion Roussel formed
1999	Aventis formed through merger of HMR with Rhone Poulenc
2004	Sanofi-Aventis Novexel spin off

Overview

- “spin-out” of the Sanofi-Aventis anti-infective group – created on 1st December 2004.
- Portfolio of antibacterial and antifungal assets transferred to Novexel S.A.
  - 21 Programmes (5 development phase)
  - >50 Patent Families
- “state of the art” facilities provided on the former Aventis site in Romainville, France
- Financial support from leading international investor syndicate

Corporate Structure

- Investor Syndicate - € 40.0 m (€ 26.9 m + € 13.1 m)
  - Atlas Venture
  - Sofinnova
  - 3i
  - Abingworth
  - Novo
- Sanofi-Aventis will hold ~ 20% of fully diluted share capital through contribution of
  - Tangibles (scientific equipment)
  - Intangibles (software and patents etc)
  - Cash

Management

Iain Buchanan	CEO	Vertex, J&J, Biogen
John Hodgson	CSO	Aventis, HMR, SKB
Manickam Rangaraju	Clinical Development	Aventis, HMR
Aram Mangasarian	Business Development	ExonHit
Gordon Waldron	CFO	Synt;em, TI

Board Composition

Goran Ando	Chairman
Denis Lucquin	Sofinnova
Francois Thomas	Atlas
Genghis Lloyd-Harris	Abingworth
Patrick Chocat	Sanofi-Aventis
David Shlaes	Independent
Iain Buchanan	CEO
John Hodgson	CSO

Vision

To build a specialty anti-infective pharmaceutical company dedicated to address the growing problem of bacterial resistance in the hospital environment

Agenda

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The Novexel Portfolio

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novel therapies for infectious disease

Programme	*Compound*	*Phase*	*Partner*
Aminocandin Antifungal	NXL 201	Phase I	Indevus
Oral Streptogramin	NXL 103	Phase I	sanofi-aventis
Topoisomerase IV inhibitor	NXL 101	Preclinical	none
ß Lactamase Inhibitor	NXL 104	Preclinical	none
Penicillin Binding Protein	various	Optimisation	none
Discovery Programmes	various	Research	none

NXL 201

Class	Echinocandin
Target	ß-(1,3)-glucan synthase
Indication	Severe Fungal Infections invasive aspergillosis disseminated candidiasis
Stage	Clinical Phase I
Partner	Indevus
Strengths	• Favourable PK profile • Fungicidal activity • Proven class • Activity against resistant strains

NXL 201 Recent Results

Excellent PK Profile	• Current *in vivo* animal studies compatible with once or twice weekly dosing: protection 7 days post treatment vs. *C. albicans in mice*[1]
Broad Activity *in vivo*	• Aspergillis spp. [2], • C. albicans • C. tropicalis, C. glabrata, C. guillermondi [3]
Activity against resistant strains *in vivo*	• Fluconazone resistant[3] • Caspofungin resistant[4] (echinocandin class)
Activity in immuno-compromised hosts	• Increased survival and reduced tissue burdens in immuno-compromised amimals[5]

[1] Poster F-496 Najvar et al ICAAC 2005; [2] F-494 & F-495 Warn et al, ICAAC 2005;
[3] Posters F-492 Girard et al; [4] Poster M-1624 & F-493 Brzankalski et al ICAAC 2005;
[5] Poster F-494 Warn et al ICAAC 2005;

NXL-201 – License

- April 2003 Agreement with Aventis assigned to Novexel
- Worldwide, exclusive license grant with right to grant sub-licenses
- Indevus to use commercially reasonable efforts to develop and commercialize product
- Joint representation on development steering committee
- Clinical development, Regulatory, and sales Milestones for oral and i.v. products
- Royalty bearing

NXL 103

Class	Oral Streptogramin
Target	Bacterial Ribosomal Inhibitor
Indication	Mild to moderate RTI
Stage	Clinical Phase I
Partner	Sanofi-Aventis (option)
Strengths	• Antibacterial spectrum • Orally bioavailable • Proven class • Low occurrence of resistance

NXL 103 Recent Results

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Bactericidal in patient serum	Serum from patients receiving single dose NXL-103 bactericidal for 6/8 S. pneumoniae strains and 8/8 vs. S. aureus strains tested[1]
Active against resistant bacteria	Not affected by beta-lactam or macrolide resistance, active against MRSA[2]
No existing resistant population	No resistant population found in 6591 clinical isolates of from EU-wide sampling of respiratory pathogens in 2003-2004[3]

[1] Poster A-225 Lowther et al ICAAC 2005;
[2] Poster F-2049 Andes et al, ICAAC 2005;
[3] Poster F-2030 Bryskier et al, ICAAC 2005.

NXL 103 Option Right

- NXL103 Subject to Sanofi Aventis option right
- Limited in time through Phase IIA outcome and different financial conditions upon exercise at
  - Phase I
  - Phase IIA
- Option fees
- Clinical Development, Regulatory and Approval Milestones (approximately € 100m)
- Tiered Royalty Rate
- Retained co-promotion right

NXL 101

Class	Novel
Target	Bacterial Topoisomerase IV
Indication	Hospital infections caused by Gram +ve pathogens including (MRSA, MRSE and pen-R streptococci)
Stage	Preclinical
Partner	Not Partnered
Strengths	• Novel mechanism • Novel chemical class (non-quinolone) • Gm +ve spectrum • Bactericidal

NXL 101 and MRSA

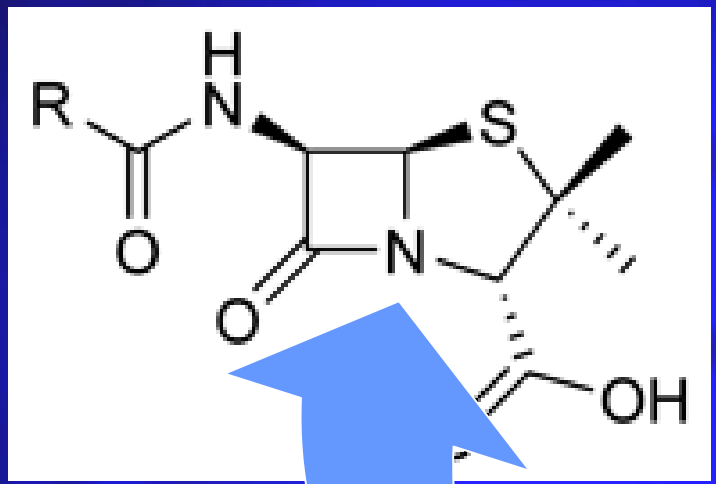
	methicillin-susceptible *Staphylococcus aureus* (n = 41)			methicillin-resistant *Staphylococcus aureus* (n = 53)		
	MIC (mg/L)					
Antimicrobial	***50%***	***90%***	***Range***	***50%***	***90%***	***Range***
NXL 101	**0.25**	**0.25**	**0.06 – 0.25**	**0.25**	**0.25**	**0.06 – 0.5**
Erythromycin A	0.25	>64	0.25 ->64	>64	>64	0.25 - >64
Pristinamycin	0.25	0.25	0.12 – 0.5	0.5	1	0.12 - 1
Teicoplanin	1	1	0.25 - 2	1	2	0.5 - 8
Linezolid	2	2	0.5 - 2	2	2	1 - 32
Moxifloxacin	0.06	0.12	0.03 - 8	2	8	0.06 - 16

Source : EECMID Poster (1159) Copenhagen 2-5 April 2005 - M.J. Robbins et al

NXL 104

Class	Novel
Target	ß-Lactamase (class A, C and ESBL)
Indication	Treatment of nosocomial infections caused by Gram -ve pathogens
Stage	Preclinical
Partner	Not Partnered
Strengths	• Novel class • Targeted spectrum • PK profile for combination with selected ß-Lactam • Combination (low resistance)

Structure of β-Lactam core

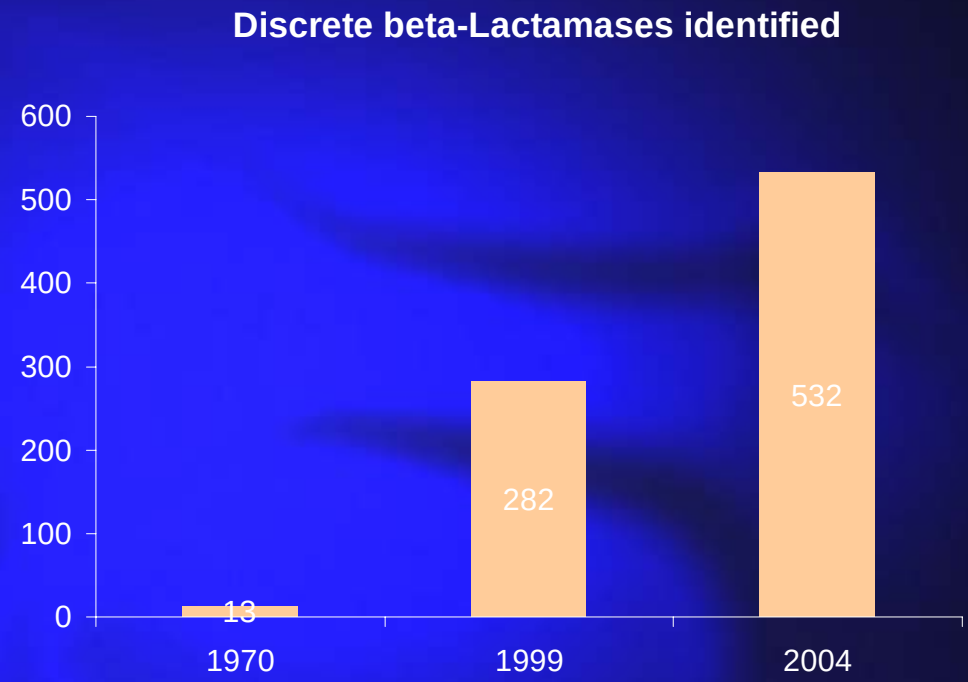


ß-Lactamase attack

NXL-104

β-lactamases cause concern

- plasmid mediated spread of AmpC cephalosporinases
- rapid evolution and spread of extended spectrum β-lactamases (ESBLs)
- evolution of carbapenem hydrolysing enzymes : Class A carbapenemases & Class B metallo-enzymes



Source : Bad Bugs Need Drugs – March 2006 – ISDA - K Bush personal communication

NXL 104 and MIC values

MIC (mg/L) - Geometric Mean

Enterobacteriaceae	*AMX*	*AMX-C*	*AMX-NXL*	*CAZ*	*CAZ-NXL*
E.coli (n=12)	>64	48	**0.21**	43	**0.2**
C.freundii (n=6)	>64	>64	**9**	114	**0.5**
K.pneumoniae (n=11)	>64	17	**1.5**	186	**0.53**
E.cloacae (n=13)	>64	>64	**18**	93	**0.85**

Note : *amoxicillin (AMX)*

amoxicillin / clavulanic acid 4 mg/L (AMX-C)

amoxicillin / NXL 104 4 mg/L (AMX-NXL)

ceftazidime (CAZ)

ceftazidime / NXL-104 4 mg/L (CAZ-NXL)

Source : EECMID Poster (1348) Copenhagen 2-5 April 2005 - J. Shackcloth et al

NXL 104 Recent Results

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In vitro Studies	NXL-104 protected cefixime and cefpodoxime from hydrolsis by TEM-3, -6, -9, -10, OXA-1 and –5 ß-lactamases[1]
Septicemia Model	ED50 range <5-29 mg/kg for ceftazadime + NXL-104 vs. >90 mg/kg for ceftazadime alone[2]
Pneumonia Model	3-6 log reduction in lung bacterial counts compared to ceftazadime alone or ceftazadime + clavulanic acid[2]

[1] Presentation F-1161 Robbins et al ICAAC 2005;
[2] Presentation F-1164 Levasseur et al ICAAC 2005

PBP Programme

Class	Various Novel
Target	Penicillin Binding Protein
Indication	Treatment of Gram +ve and Gram -ve nosocomial infections including drug resistant strains
Stage	Chemical Optimisation
Partner	Not Partnered
Strengths	• Novel class (not ß-Lactam) • Known target • Extended spectrum

Problem Pathogens

Pathogen	Novexel Solution
A. baumannii	-
Aspergillus spp.	NXL-201
ESBL producing Gm-ve	NXL-104
Vancomycin-R *E. faecium*	NXL-104
P. aeruginosa	NXL-104, PBP inhibitors
MRSA	NXL-101

Source : "Bad Bugs need Drugs" - ISDA Report - March 2006

Agenda

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Milestones

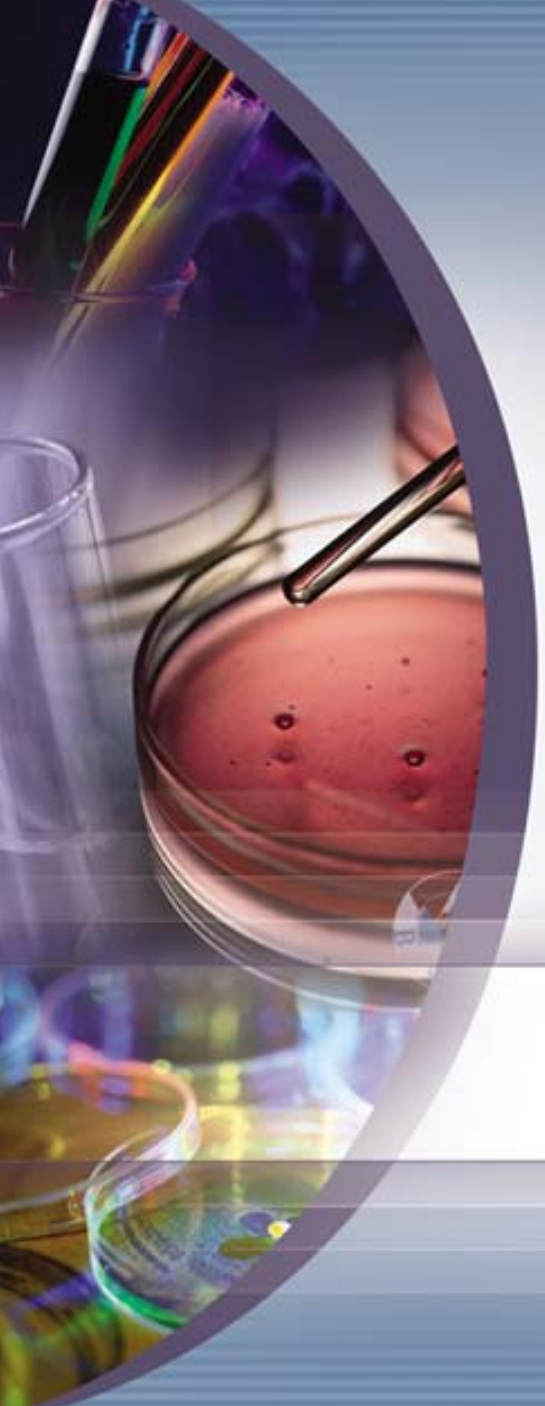
- Pipeline Advancement
  - NXL-201 to Phase II – 1H 2007
  - NXL-101 to Phase I – 2H 2006
  - NXL-104 to Phase I – 2H 2006
  - NXL-103 to Phase II – 2H 2006
- Pipeline Enhancement
  - In-license of additional compound(s)
  - New Development Candidate – PBP
- Out-license agreements
  - Exploratory discussions NXL-104 / NXL-101

Novexel - Pipeline end-2006

Compound	Indication
NXL 201	Severe Fungal Infection
NXL 103	Respiratory Tract Infections
NXL 101	Hospital Gram + infections
NXL 104	Hospital Gram - infection
PBP Inhibitor	Hospital Gram +/- infections

Highlights

- Broad portfolio of well-defined programmes with a specialised anti-infective focus
- Hospital sector represents significant market with need for novel class compounds
- Experienced management team with key skills in anti-infective R&D
- Appetite for late stage anti-infective assets in 2005



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