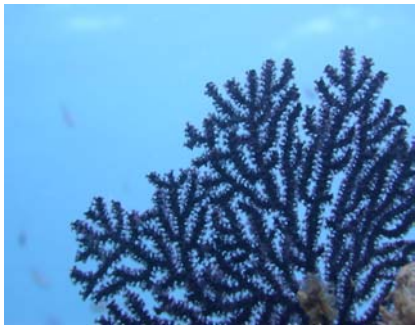


Business Review Day

Colmenar Viejo
Wednesday, 28th January 2004

Pharma Mar

Business Review
28 January 2004

Presentation Team and Agenda

12:45	PharmaMar Strategic Approach	I Lozano, Chief Executive Officer
13:45	Preclinical Pipeline	C Cuevas, Director of Research and Development
14:15	Break	
14:45	Clinical Pipeline	MA Izquierdo, Director of Clinical Development
15:45	Financials	ML de Francia, Group Finance Director, Zeltia S.A.
16:15	Closing Remarks and Final Q&A	I Lozano and team

PharmaMar Strategic Approach

Isabel Lozano
PharmaMar CEO

Overview

- PharmaMar today
- Yondelis™ appeal
- Business plan - impact on activities and goals
- Status of our projects
- Conclusions

Mission

"To advance Cancer Care through the discovery and development of new marine-derived drugs"

PharmaMar Today

Clinical pipeline

- 4 drugs under active clinical development
- New drug to enter clinical trials within a year
- Not a "one product, one technology company"

Preclinical pipeline

- Many new families of preclinical compounds
- Three compounds in advanced stages of development
- Largest marine library for drug discovery

Intellectual property

- 580 issued patents with new applications filed every month

Co-development and commercialization partnership

- J&J for Yondelis™

Resources

- Solid team of professionals in the US and Europe
- Backing of the Zeltia Group

Yondelis™ 3rd Line in STS / CPMP Opinion

Side by side comparison of quotes from EMEA opinion and divergent opinion

COMMENTS	CPMP OPINION (14 VOTES IN FAVOUR)	DIVERGENT OPINION (12 VOTES AGAINST)
DISEASE	**Difficult** to conduct **clinical trials** in STS **Large series** of data presented in the context of this rare disease	STS is a **rare** and **life-threatening** disease Remains a **large medical need**
METHODOLOGY	**Critical concerns** Resulting **potential bias**	**Some** problems A **careful analysis** of the data observed leads us to believe that the observed **affect is real and consistent**
ACTIVITY	**Considerable uncertainty** about: • the level of **Response Rate** • **progression-free survival** • **overall survival rates**	**Clinically relevant effect in a significant proportion of patients:** • the **Response Rate** observed is considered relevant • **significant proportion of patients showed** PFS at 6 months (progressive disease documented at entry) • unexpectedly **high proportion** of patients with **long-term survival** was observed
EFFICACY	**Could not be established**	**Has been demonstrated** in the proposed indication
TOXICITY	NO CPMP COMMENT	Significant but manageable
CONCLUSION	Its previous opinion of 24 July 2003 recommending the refusal of the granting of the Marketing Authorisation for Yondelis should not be revised	The benefit/risk balance for Yondelis is positive /../ it could be given an approval under exceptional circumstances

Yondelis™ Status
A Broad-spectrum Antitumoural

- SAFETY has been demonstrated
- EFFICACY has been demonstrated in a setting where no alternatives are available and data in other settings warrants rapid development of the drug
- Clinical development rapidly progressing within the Joint Dev. Plan

Therefore:

- The EMEA opinion has no impact on continued development of Yondelis™ or on the rest of the pipeline
- We are confident that Yondelis™ will be successful in its target indications

Strategic Objectives for 2004-2006

- Register Yondelis™ in Europe in 2006
- Stretch current cash resources to achieve this registration
- Sell Yondelis™ in Europe
- Enter into co-development agreements at the appropriate time to maximise value of both clinical and preclinical pipeline
- Feed clinical pipeline with innovative candidates: a new compound every two years

Tactics

- Focus on clinical and advanced preclinical drug development programs
- Save costs through optimization in:
    - Early stage discovery
    - Manufacturing
    - Sales and marketing
- Maximise value of our pipeline through partnering and prioritisation of advanced preclinical pipeline
- Preserve core strengths and critical mass
- Leverage resources of the Zeltia Group

Clinical Development

Focused development and registration strategy

- Expand drug profile through schedule optimization and combination therapy development
- Development driven by market opportunity, medical need and regulatory criteria
- Increase development speed through accelerated recruitment and center openings

Optimize activities

- Team reorganization and reinforcement (9% headcount increase in 2004)
- Increase investment (38% budget increase in 2004)

Next major milestone: Yondelis™ launch in 2006

Preclinical & Drug Discovery

Core objectives and goals are maintained

- Generate innovative clinical candidates with new modes of action
- Maintain rate of entry of new molecules in clinic: one every 2 years

While operation is optimized

- Budget reduced by 40%
- Investment on advanced preclinical pipeline maintained
- Compensate reduced investment on early stage projects by opening drug discovery pipeline to partnering
- Capacity to renew pipeline within planned budget

Strong and diverse preclinical pipeline

Manufacturing

Manufacturing strategy remains unchanged

- Retain control over key steps in active ingredient manufacturing
- PharmaMar sole worldwide supplier

Optimization of operations

- Cost reductions of 57%
- Complete switch from natural source to synthetic production of Yondelis™ in 2004
- Input from FDA:
  - Accepted strategy for switch to synthetic Yondelis™
  - No bridging clinical trials required

Industrial-scale production assured

Sales, Marketing and BDL

Maintain strategic objectives

- Retain commercial rights in EU

Optimize activities

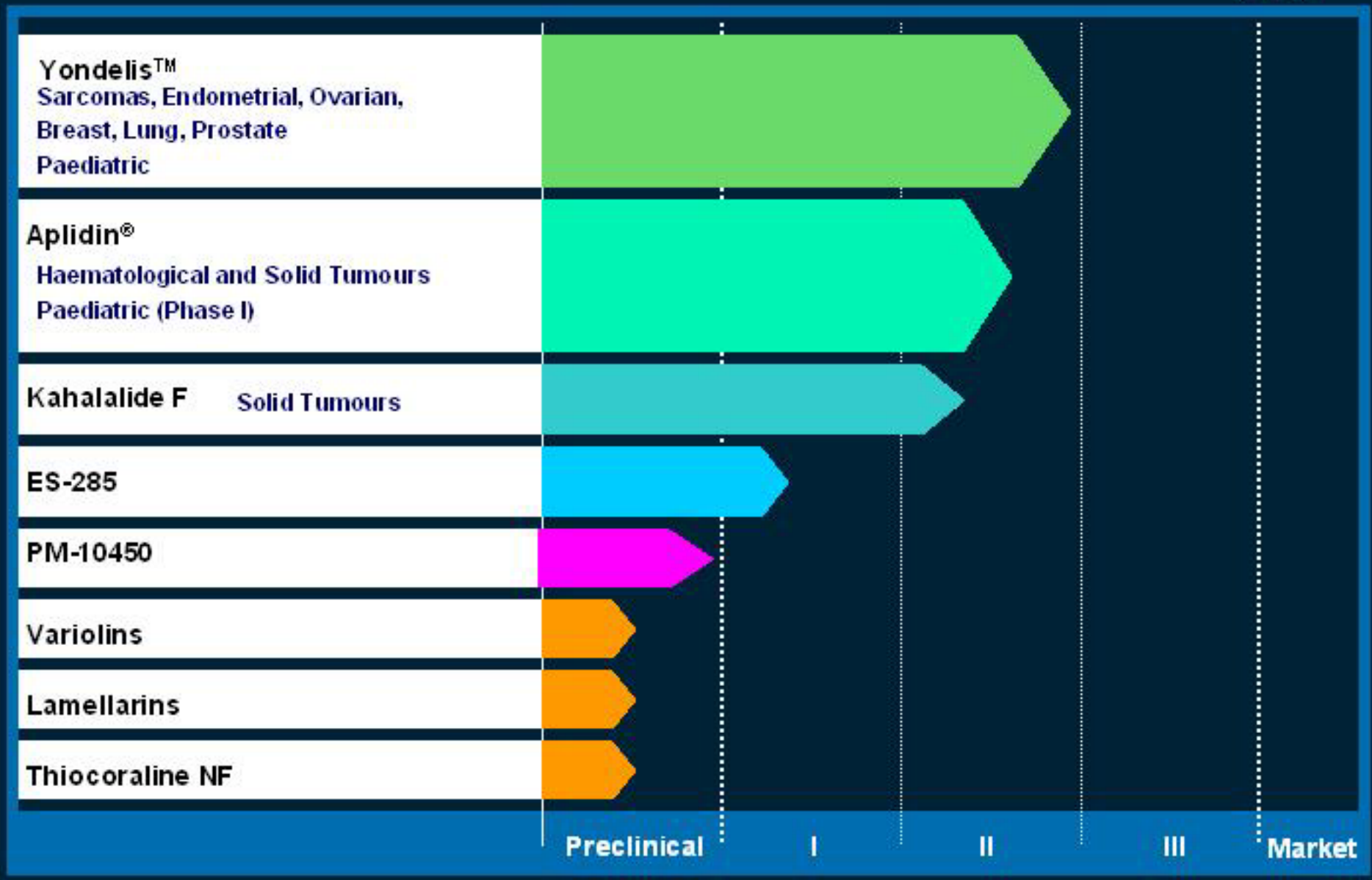
Retain key expertise to:

- Maintain network with key opinion leaders
- Reinforce market orientation of drug development projects
- Support business development
- Generate income (€ 60 m forecast 2004-06)

Closure of commercial activities

- 74% expenditure reduction

Our Oncology Pipeline



Yondelis™ Clinical Summary

Single agent

- Phase II paediatric trial under preparation
- 8 Phase II trials:

Soft Tissue Sarcoma	3 in Ovarian Carcinoma	Endometrial
Breast	NSCLC	Prostate

Combination studies

- 9 Phase I trials:

2 with Doxorubicin	Doxil ®
Cisplatin	Carboplatin
Paclitaxel	Docetaxel
Gemcitabine	Capecitabine

Yondelis™ Joint Development Plan (JDP)

J&J / PharmaMar

- JDP includes all indications and combination trials
- 65% of all Yondelis™ development costs paid by J&J
- J&J pays for active ingredient
- Common regulatory strategy for both territories
- First registration expected in EU in 2006

Yondelis™: Size of the Opportunity

Worldwide estimates

	STS	OVARIAN	ENDOMETRIAL	NSCLC	BREAST	PROSTATE
New cases/year 2000 (1)	79,368	192,379	188,952	929,145	1,050,346	542,990
Treatment (2)	Doxorubicin Ifosfamide	Taxol Carboplatin Caelyx Topotecan Cisplatin		Taxol Carboplatin Cisplatin Taxotere Gemzar Navelbine Iressa	Doxorubicin CMF 5 FU Taxol Taxotere Herceptin Xeloda Myocet Epirubicin	Hormonal therapy Novantrone
Market Forecast 2007(3)	$ 153 M †	$ 517 M	$ 162 M†	$ 1.2 B	$ 4.1 B	$2.4 B

(1) Incidence Globocan 2000. STS from CEDA database 2000
(3) Cancer Therapy WW Market Survey, ADIS International May 2001.

(2) Approved therapies only
† *Company Estimates;*

Aplidin® Clinical Summary

Solid Tumours Adult and Paediatric

- 10 exploratory small population Phase II trials to define target indication:

2 in Colon / Renal	Pancreas	Bladder
Prostate	NSCLC	Medullary Thyroid- MTC
SCLC	Head & Neck	Melanoma

Haematological Tumours Adult and Paediatric

- 4 Phase II trials:

Multiple Myeloma	Adult Acute Leukaemias
Low Grade NHL	High Grade NHL

Kahalalide F Clinical Summary

- Phase I dose regimen study ongoing (schedule optimization)
- Phase II trial ongoing — Hepatocarcinoma
- Two Phase II studies under preparation — Melanoma; NSCLC

Aplidin® and KF: Size of the Opportunity

Worldwide estimates

	MELANOMA	BLADDER	SCLC	PANCREAS	H&N	RENAL
New cases 2000 (1)	132,602	335,795	309,521	332,034	331,468	160,715
Treatment (2)	Intron A	Cisplatin Valrubicin	Etoposide P VP-16 Topotecan	Gemzar		Proleukin
Forecast 2007 (3)	$728 M	$348 M †	$417 M	$1.2 B †	$284 M	$310 M†

	NSCLC	PROSTATE	M. MYELOMA	LEUKEMIAS	HEPATOCARCINOMA
New cases 2000 (1)	929,145	542,990	73,943	257,096	564,336
Treatment (2)	Taxol Carboplatin Cisplatin Taxotere Gemzar Navelbine Iressa	Hormonol therapy Novantrone	Melphalan Prednisone Vincristine Doxorubicin Velcade	Gleevec Leukeran Leustatin Daunorubicin Fludara Mylotarg Idarubicin Intron A Novantrone Nipent Vumon	
Forecast 2007 (3)	$1.2 B	$2.4 B	$945 M †	$789 M	$205 M

(1) Globocan 2000
(3) Cancer Therapy WW Market Survey, ADIS International May 2001

(2) Approved therapies only
† Company Estimates

ES-285

- 4 Phase I trials ongoing in solid tumours with different dose regimens
  - 3 hrs / d x 5 / 3 weeks
  - 24 hrs / 3 weeks
  - 3 hrs / 3 weeks
  - 3 hrs / weekly

Reduction in Total Expenses

Amounts expressed in € m

	PRE-CLOSING					
	2003	2004	04 *vs* 03	%	2005	2006
R&D	22.7	14.3	-8.4	-37%	14.8	15.4
CLINICAL	10.7	14.8	4.1	38%	17.3	13.3
INDUSTRIAL	14.9	6.4	-8.5	-57%	4.2	4.4
REGULATORY	1.5	1.6	0.1	7%	1.7	1.7
COMERCIAL OPS.	10.3	2.7	-7.6	-74%	4.0	6.0
GENERAL & ADMIN.	3.7	2.8	-0.9	-24%	3.0	3.1
TOTAL EXPENSES	63.8	42.6	-21.2	-33%	45.0	43.9

Headcount

- Cost of redundancies:
  - Fully paid up in 2003
  - 6.5 month payroll cost equivalent
- Total personnel today: 215
- Preserving expertise and critical mass in key areas, with capability to achieve objectives

Headcount 2004

- Preserving expertise and critical mass in key areas, with capability to achieve objectives

	Headcount 2004
R&D	89
CLINICAL & REG.	50
INDUSTRIAL OPS	46
MARKETING & BDL	13
GEN., ADMIN & FIN,	17
TOTAL	215

Reducing cash burn

- One-off 33% reduction in annual cash burn
- Cuts completed by end 2003
- Targeted reductions safeguarding and reinforcing highest priority projects
- No further reductions required to deliver business plan / stable expenditure in 2004-2006

Cash-in-hand stretched to a total of 3 years

Summary

- Business strategy reaffirmed using a streamlined business plan
- Rapid implementation of adjustments – substantial savings achieved
  - Clinical: increased investment to focus on speedy development
  - R&D: more selective development of early pipeline with no impact on advanced projects
  - Marketing & Commercial: closure of most activities, retaining key business development support
- Business plan objectives, including first registration in 2006, achievable without additional capital increase

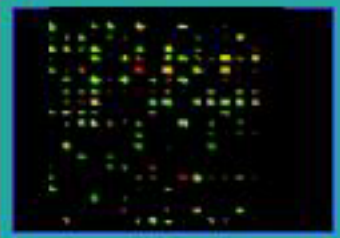
Pharma Mar

Preclinical Pipeline

Carmen Cuevas PhD
Research Director

PharmaMar Strategy for Discovery

Search the sea as a source of natural and chemical diversity to discover new drugs for the treatment of cancer

NATURAL LIBRARIES	NEW MOLECULES	COMPLEX ASSAY SYSTEMS	DEFINED TARGETS	CLINICAL TRIALS
				

R&D Process at PharmaMar

Objective: One new compound in the clinic every two years

In vitro

Building and screening the richest library of marine samples in the world

Supply

Fast establishment of molecular structures, synthetic processes and generation of a powerful collection of active molecules and derivatives

Efficacy

Rapid evaluation in human tumors in whole animal systems

Toxicology

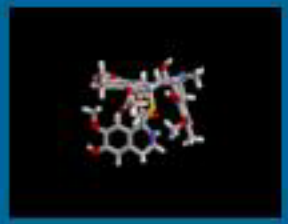
Early selection of the best clinical candidates based upon criteria of: activity / toxicity ratio, industrial drug supply and intellectual property position

Clinic

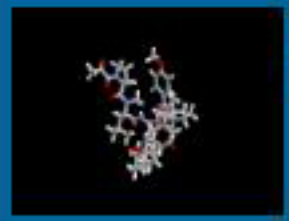
Efficient selection and preparation of the development compounds following regulatory guidelines for clinical trials

PharmaMar´s Innovative Agents

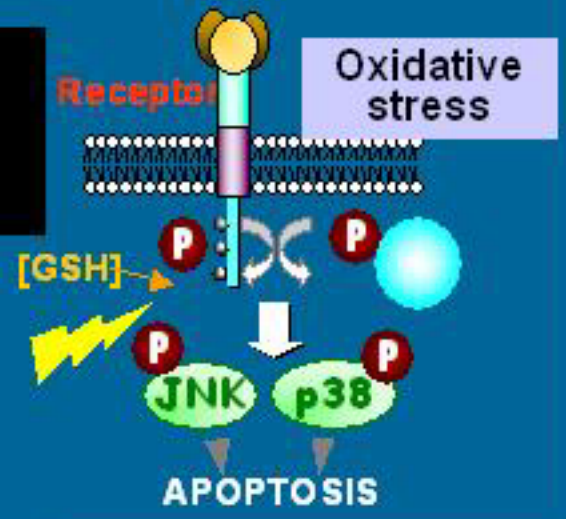
DNA repair



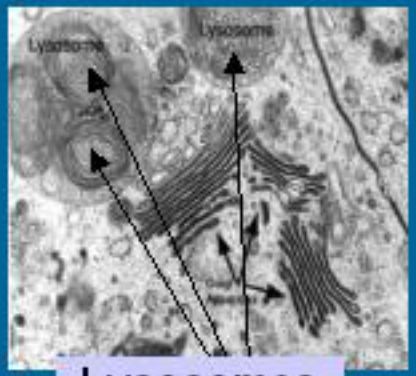
Yondelis



Aplidin

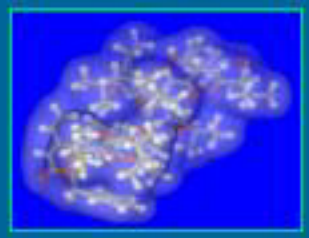


Novel Molecules with Unprecedented Modes of Action



Lysosomes

Kahalalide - F



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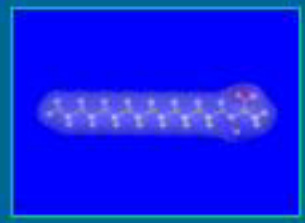
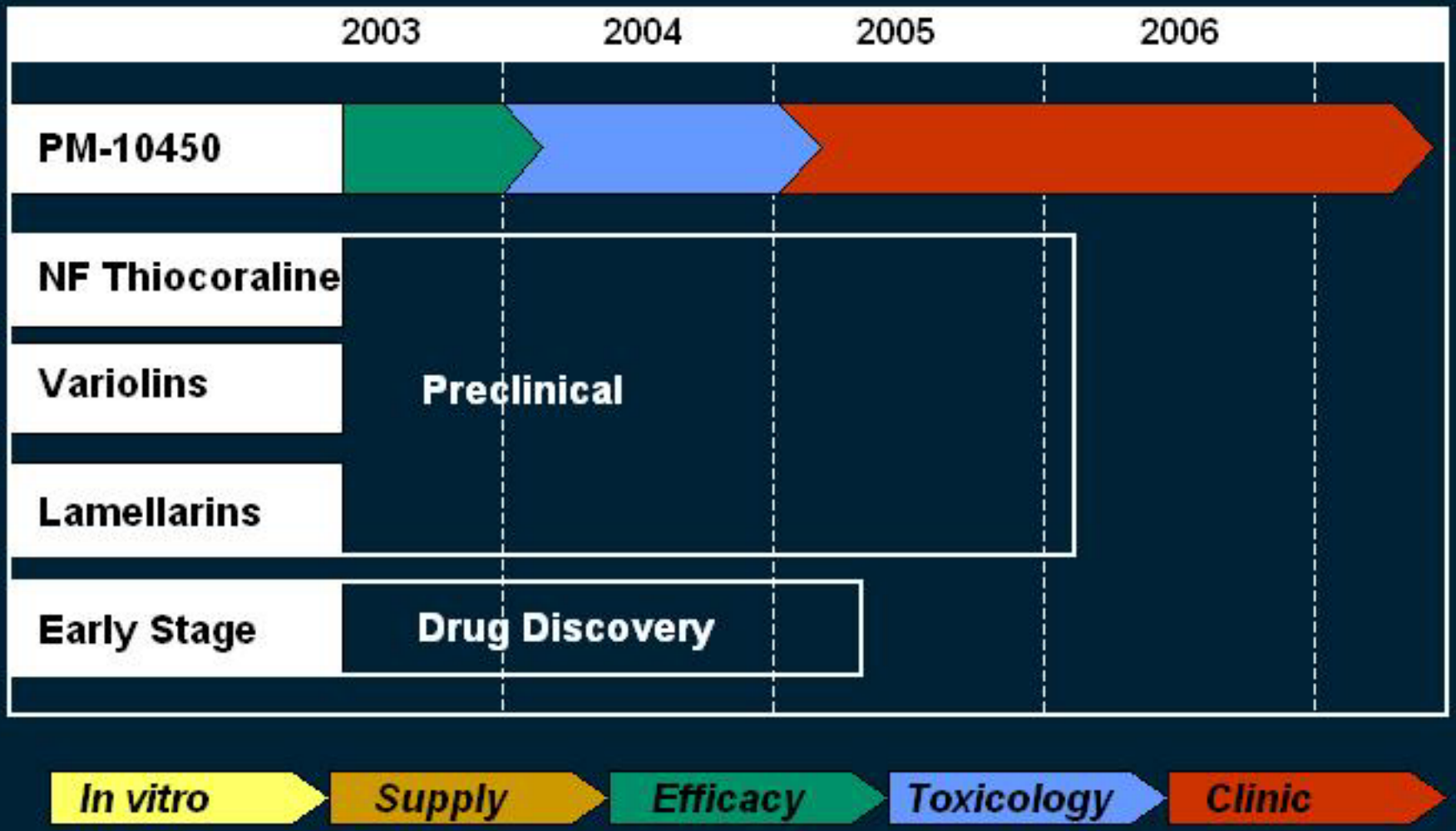


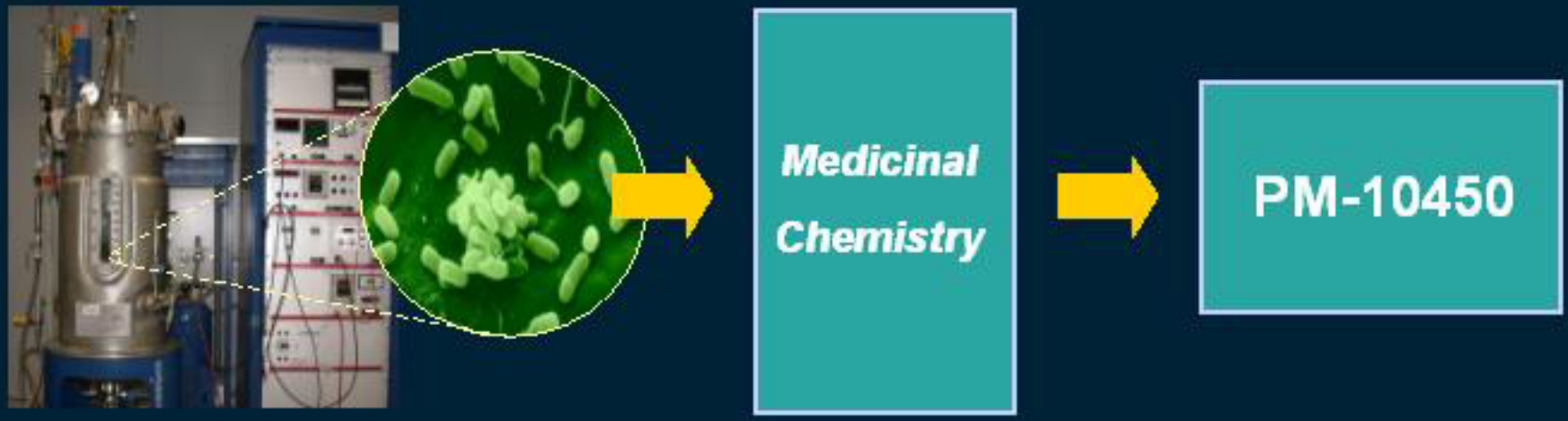
Cytoskeleton control

Advanced Preclinical Pipeline

PM-10450 clinical trials to start within a year



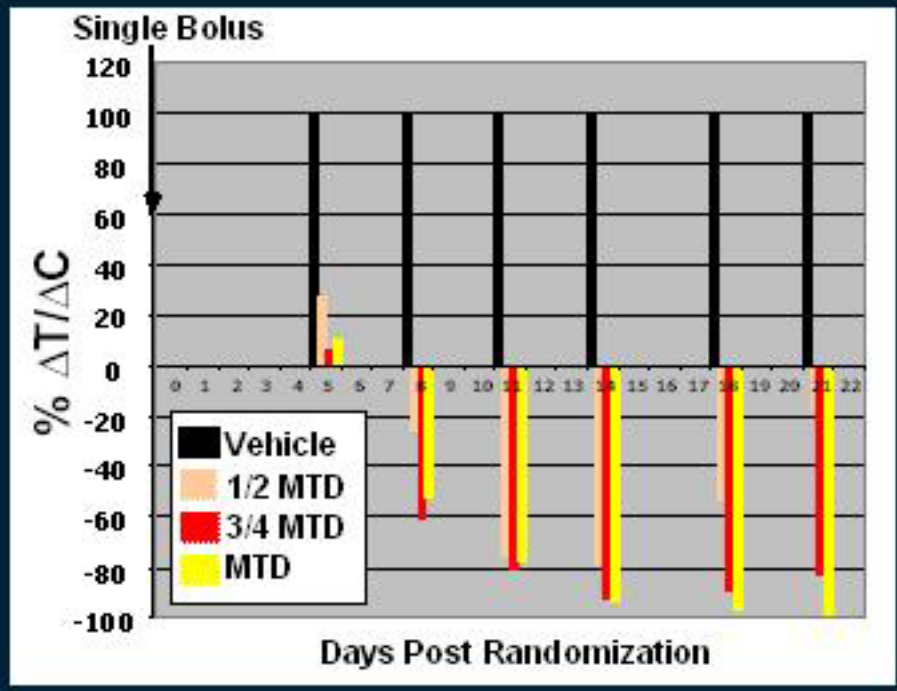
PM-10450 – In the Clinic Within a Year



- New Chemical Entity
- Novel low molecular weight alkaloids
- Easy, stable and cost effective formulation
- Scalable production process in place

PM-10450 – Preclinical Activity

- Lead candidate selected on the basis of potent *in vivo* activity
- Planned to enter the clinic within a year
- Broad spectrum of activity in animal models
- Cell cycle blockage at S and G2/M
- Lead compound currently undergoing toxicology studies

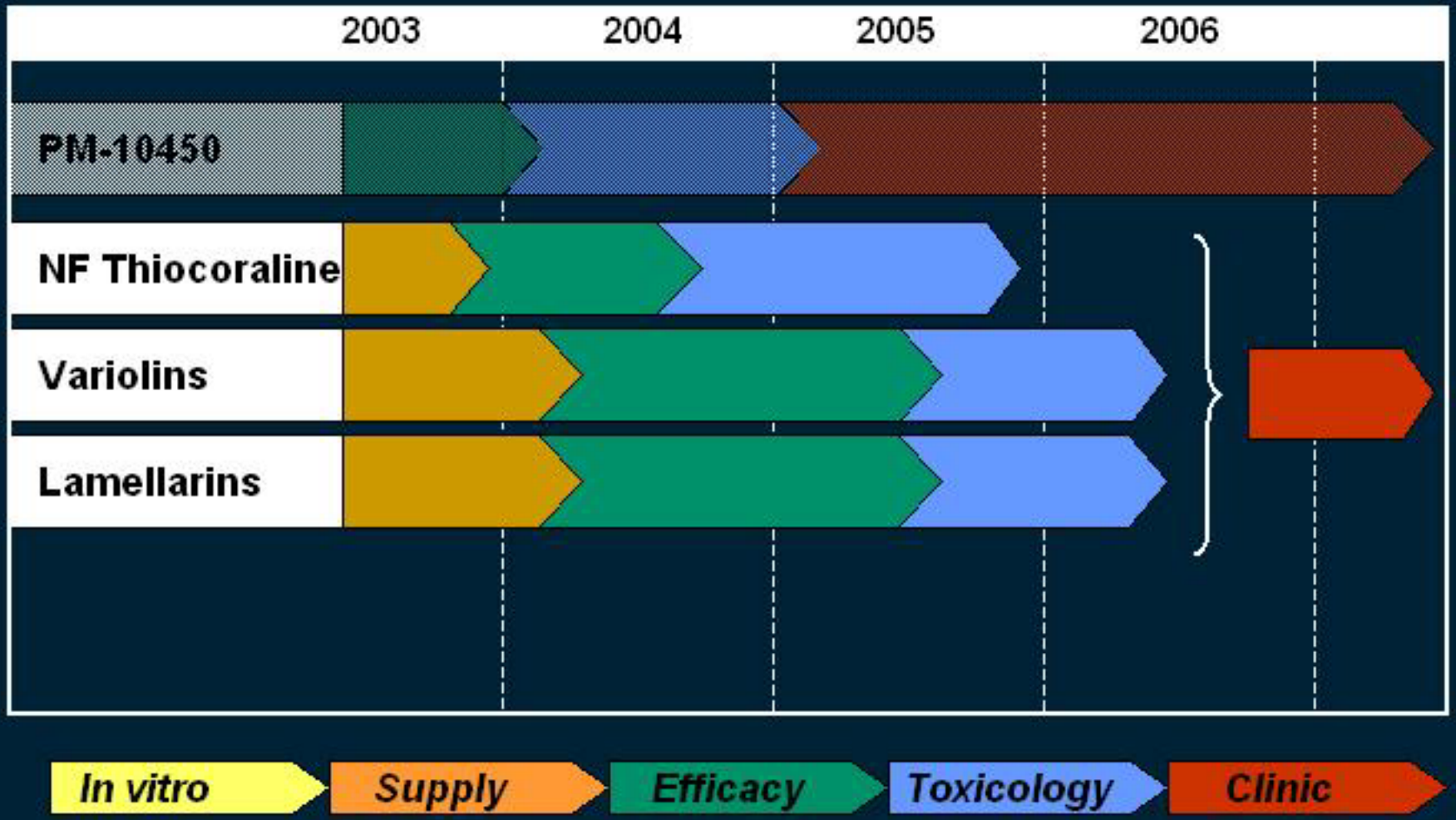


Therapeutic Index in Human Breast Tumors

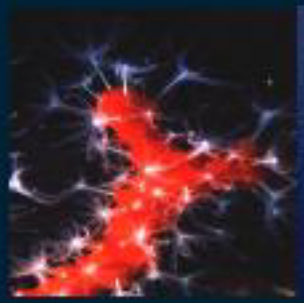
Human Breast Xenografts Qdx1, IV. Day 22

Preclinical Pipeline

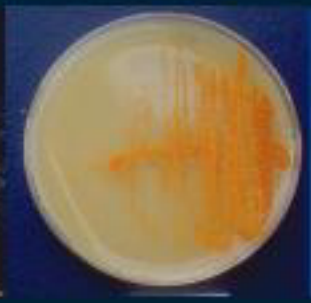
Three further candidates after PM-10450



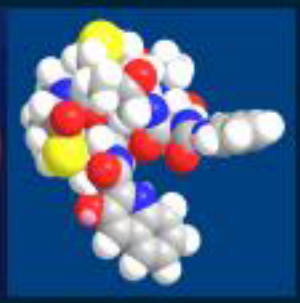
Thiocoraline NF

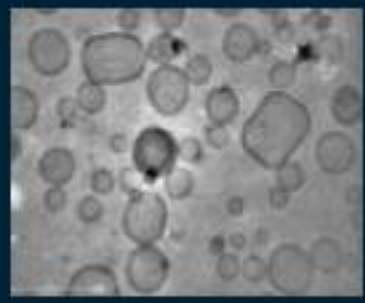


Indic Anthozoan



Micromonospora ACM2





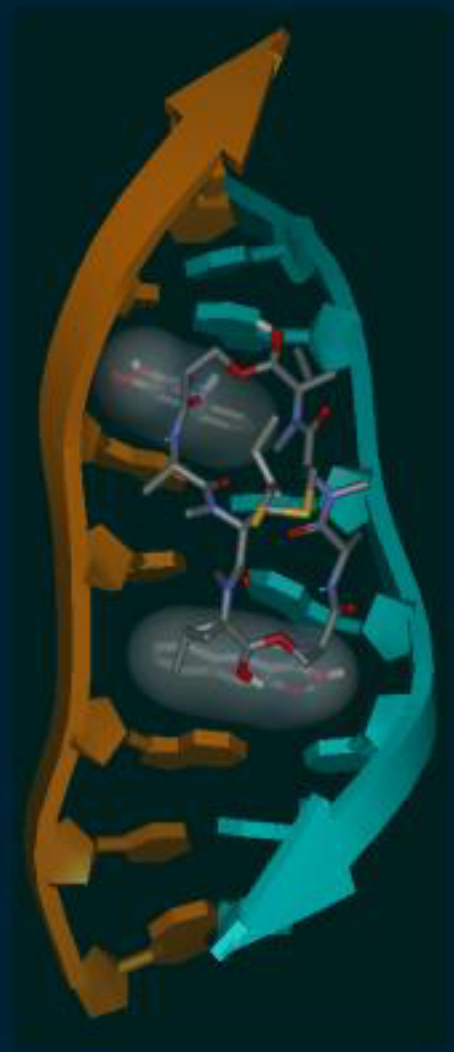
New Formulation

- Originated from a microorganism found in an Indian Ocean coral
- Genes responsible for biosynthesis characterised
- New effective lipid-based formulation
- Scalable fermentation production process

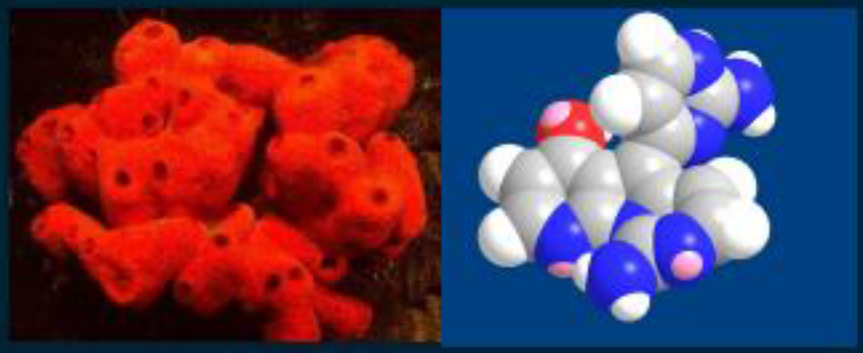
- Mode of action of thiocoraline, a natural marine compound with anti-tumour activity (1999) Br J. Cancer Vol 80 (7). Pp 971-980
- Total Syntheses of Thiocoraline and BE-22179 and Assessment of Their DNA Binding and Biological Properties. (2001) J Am Chem. Soc. Vol. 123 (4). pp561-568
- Validation of a sensitive assay for thiocoraline in mouse plasma using liquid chromatography-tandem mass spectrometry (2003) J Chromatogr B Analyt Technol Biomed Life Sci. Volume 794 (1) , pp89-

Thiocoraline NF – DNA Intercalator

- *In vitro* activity in low nM range against a broad spectrum of tumour cell lines
- New formulation confers potent antitumour activity against human tumours in animal models
- DNA bis-intercalator agent, inhibitor of DNA alpha polymerase



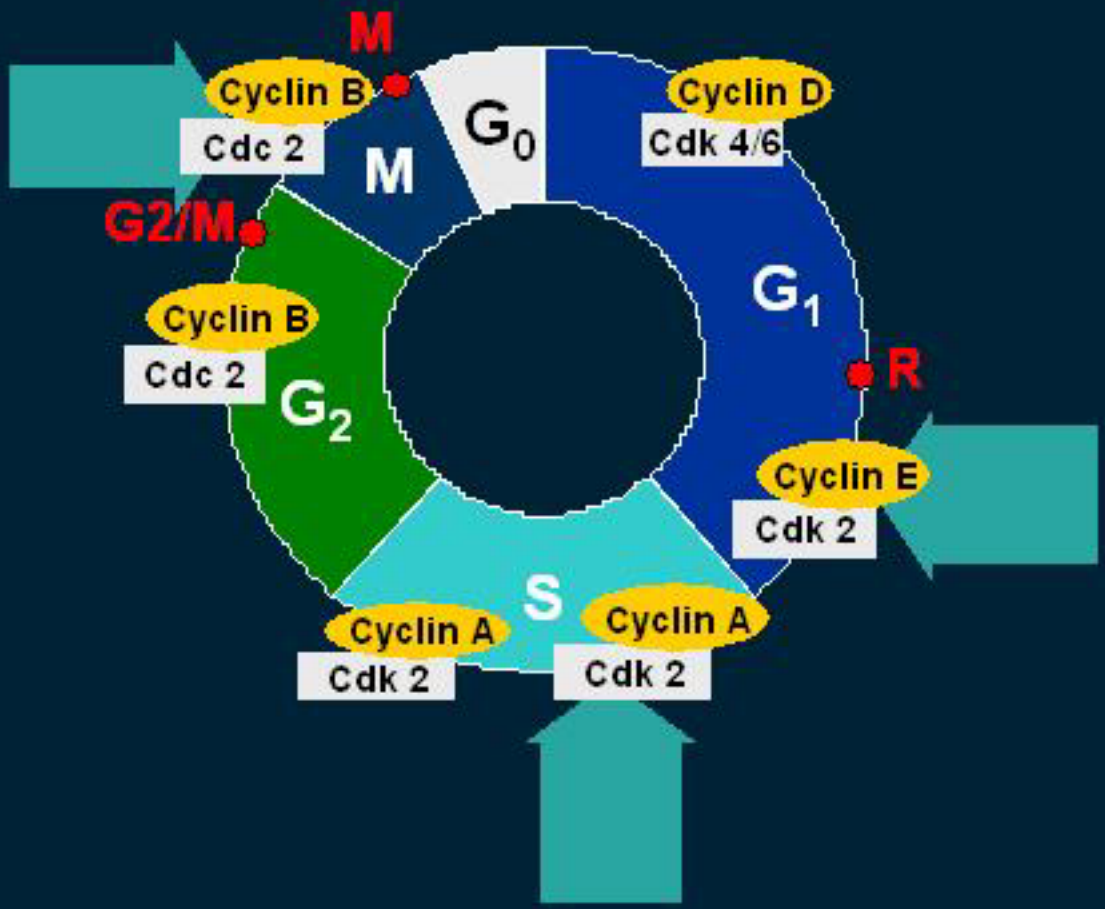
Variolins



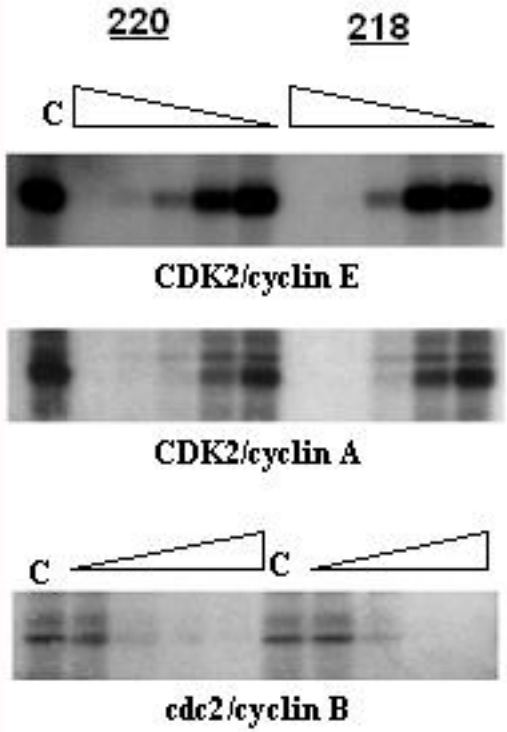
- Parent compound discovered in sponge from the Antarctic Ocean
- Inhibitors of key kinases controlling cell cycle division
- Potent induction of apoptosis, independent of p53 and MDR
- Tumour growth inhibited in human lung, ovarian and colon tumours transplanted into mice with a good therapeutic window

- Cell cycle perturbations and apoptosis induced by the novel marine compound Variolin B. (2002) European Journal of Cancer Vol. 38, Suppl 7, November 2002, page 33: 14th EORTC-NCI-AACR Symposium on "Mol Targ and Ther Frankfurt, Germany.
- Synthesis of variolin B. (2003) Tetrahedron Letters Vol 44(33). Pp 6191-6194
- Mechanism of action of Variolin B (PM01220) and its derivate deoxy-Variolin B (PM01218) (2003) AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics; Hynes Center, Boston.

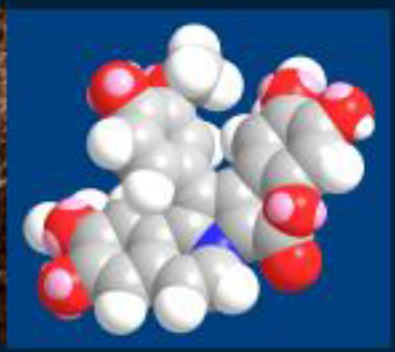
Variolins – Cdk Inhibitors



Inhibition of kinase activity of Cdk/Cyclin complexes by Variolins



Lamellarins



- Family of compounds found in ascidians
- Synthesis accomplished with scalable production
- Specific inhibitors of Topoisomerase I, a key target for cancer therapy
- Active *in vitro* against tumor cells resistant to standard Topo I inhibitors
- Blocks cell cycle at G2/M
- Blocks MDR activity

- Synthesis and structure-activity relationship study of lamellarin derivatives. (2002) J Nat Prod. Vol. 65 pp500-504
- Lamellarin D: A Novel Potent Inhibitor of Topoisomerase J. Cancer Res (2003) Vol.63 pp7392-7399
- Lamellarin D: A novel pro-apoptotic agent from marine origin insensitive to P-glycoprotein-mediated drug efflux. (2003) AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics; Hynes Center, Boston.

Lamellarins – Topoisomerase I Inhibitor

Unique and different from existing Topo I inhibitor drugs

Lamellarin – DNA – Topo I aduct.

Reversal of MDR (doxo resistance)

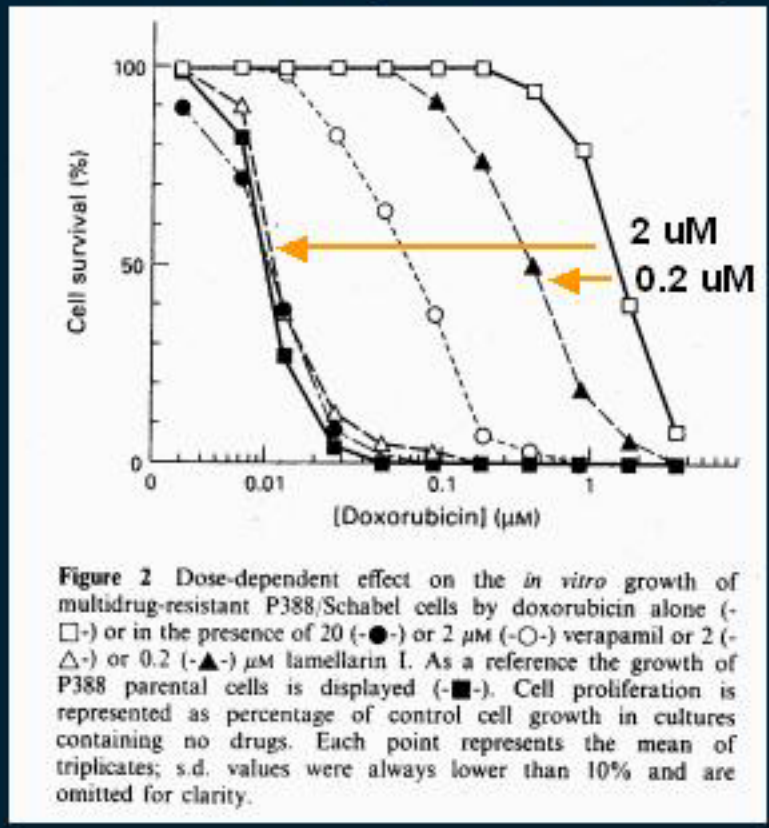
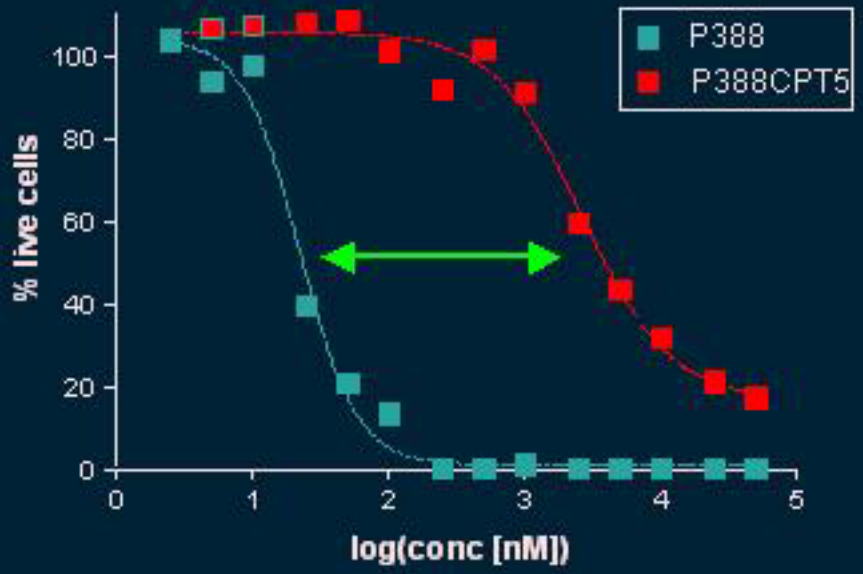


Figure 2 Dose-dependent effect on the *in vitro* growth of multidrug-resistant P388/Schabel cells by doxorubicin alone (-□-) or in the presence of 20 (-●-) or 2 μM (-○-) verapamil or 2 (-△-) or 0.2 (-▲-) μM lamellarin I. As a reference the growth of P388 parental cells is displayed (-■-). Cell proliferation is represented as percentage of control cell growth in cultures containing no drugs. Each point represents the mean of triplicates; s.d. values were always lower than 10% and are omitted for clarity.

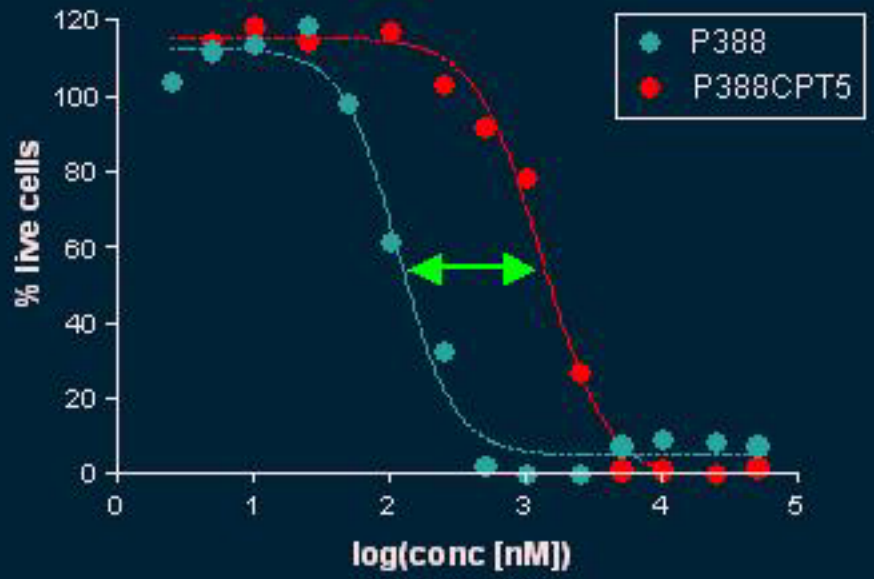
Lamellarins – *In vitro* Activity

Lamellarins show activity in cells resistant to conventional Topo I inhibitors

Treatment with CPT-11 (camptothecin)



Treatment with Lamellarin 519

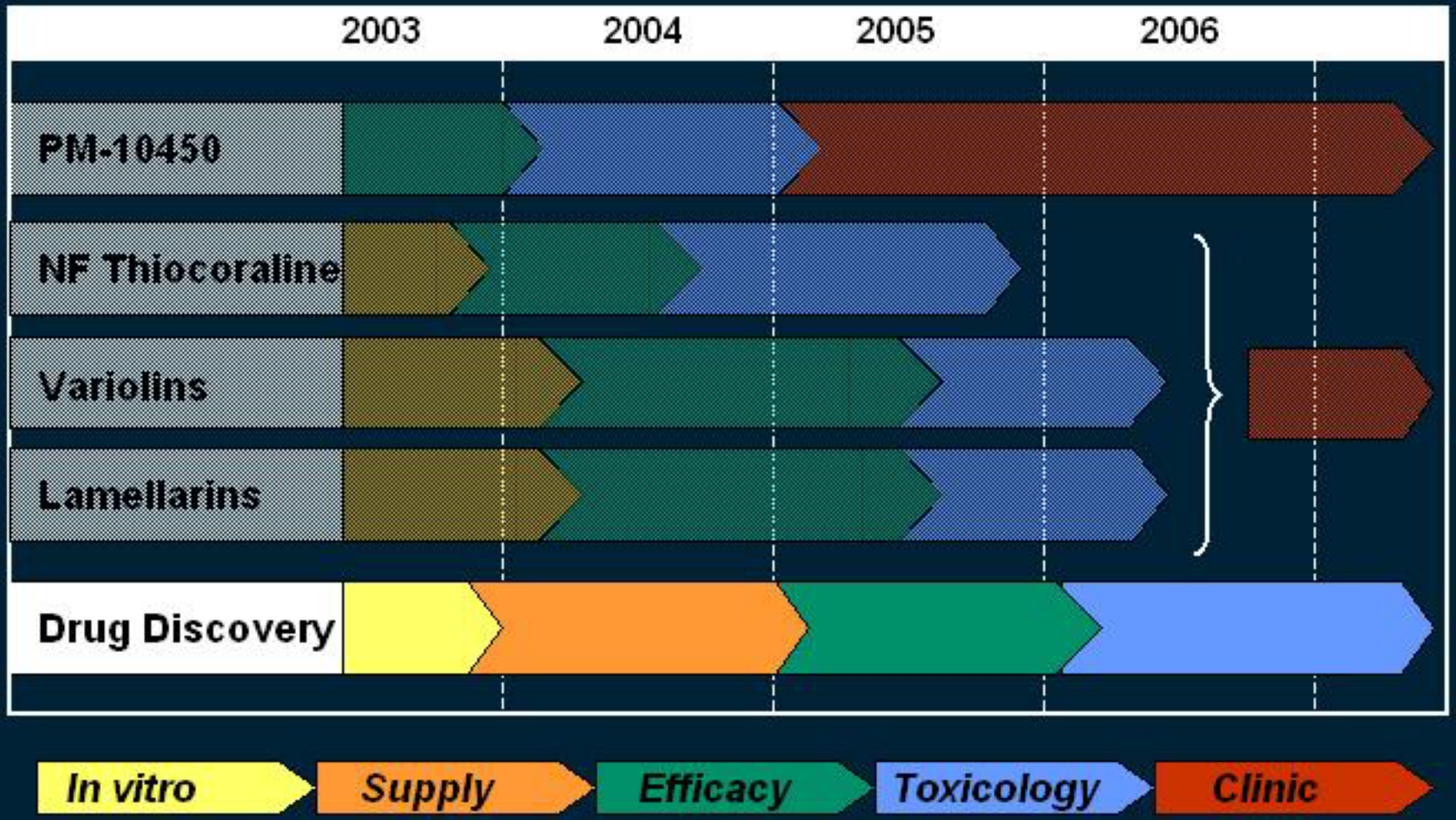


IC50 (nM)	P388	P388/CPT5	*RRI*
CPT	24	3980	168
519	136	1482	11

P388 murine leukemia cells: sensitive to Camptothecin (Conventional Topo I inhibitor)
P388CPT5 cells camptothecin-resistant, two point mutations in the *top* I gene (Gly361Val and Asp709Tyr)

Drug Discovery Pipeline

Active Drug Discovery programs to feed Preclinical Pipeline



Drug Discovery Programs

Pharma Mar

NEXT PRECLINICAL CANDIDATES

DRUG DISCOVERY	9 families of compounds prioritised for further preclinical studies. Selection based on: • Intellectual property • Structural novelty • Mode of action • Supply feasibility • Therapeutic index 40% pipeline renewal since 2000
DE-PRIORITIZED	**5 families of compounds de-prioritized**

Objectives and Resources

- Focus on accelerating PM-10450 preclinical development
- Continue strong support of compounds in clinic and advanced preclinical pipeline
- Reduce rate of sample collection and focus on exploiting accumulated library
- Selective investment in Drug Discovery projects with 37% budget reduction
- Strongly motivated R&D team of 89
- Regular flow of products into the clinic

Key Messages

- Strong and diverse preclinical pipeline
- PM-10450 : Lead candidate to enter the clinic within one year
- Investment in DD in last 3 years resulted in:
  - **Higher yield of new development candidates**
  - **Capacity to renew pipeline within planned budget**
- Exceeding our commitment to put a new compound in the clinic every two years

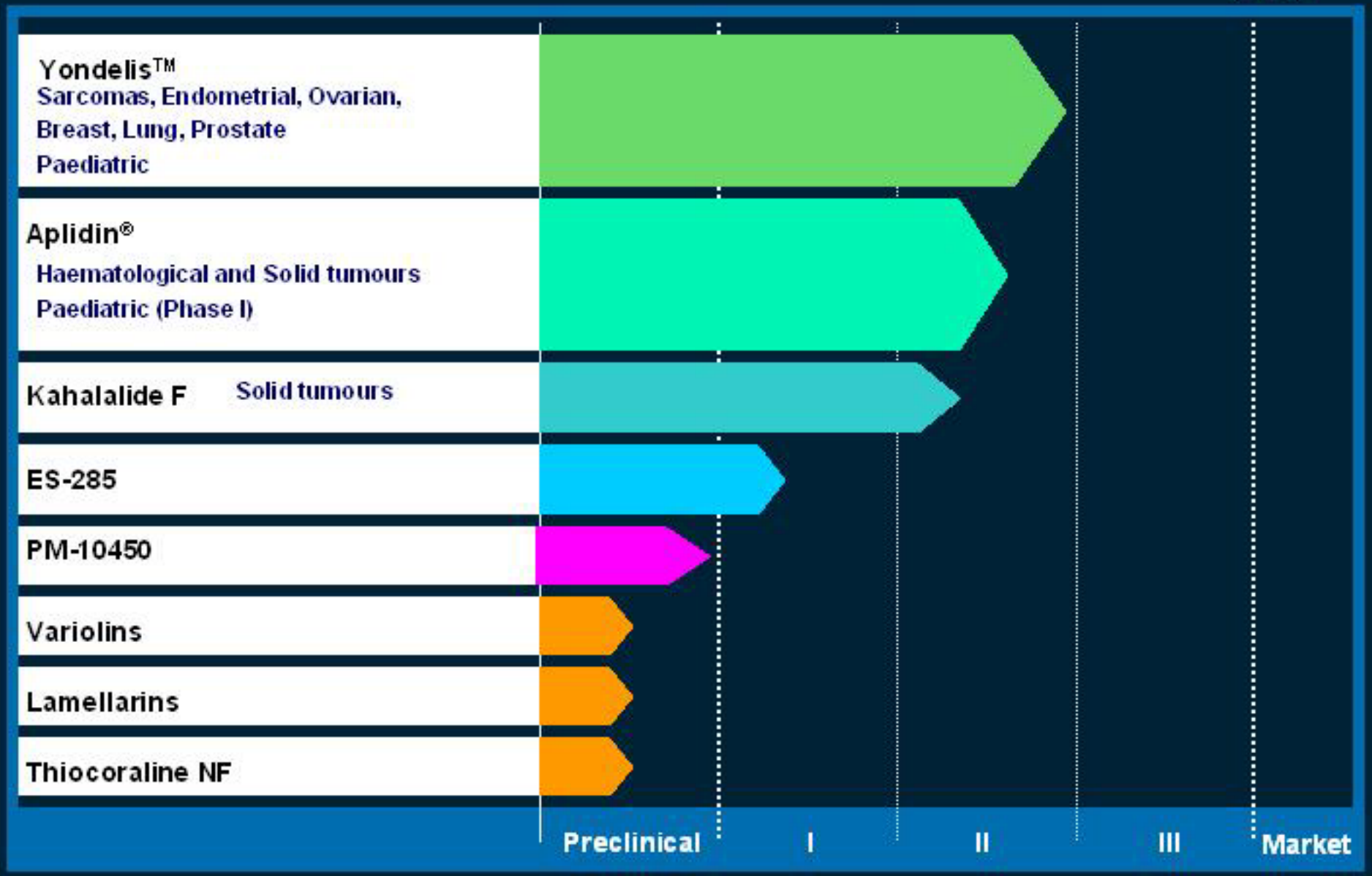
Increased R&D Productivity

Pharma Mar

Clinical Development

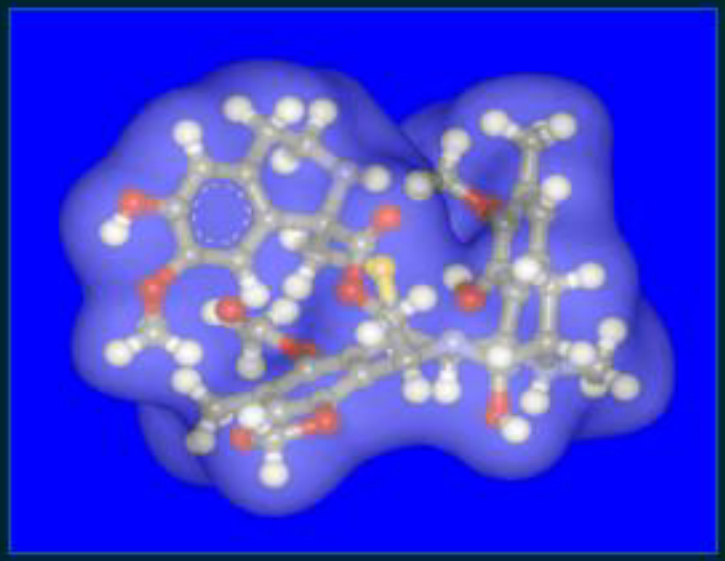
Miguel Angel Izquierdo
Director of Clinical Development

Our Oncology Pipeline



Yondelis™ (ET-743, trabectedin)

Yondelis™ – Structure & Mode of Action



- MINOR GROOVE BINDER unique in that it binds in the minor groove bending towards the major groove
- TC-NER - Transcriptional-coupled nucleotide excision repair induced cell death
- CELL CYCLE BLOCK, slowing progression through S phase and G_2/M cell cycle arrest
- TRANSCRIPTIONAL ACTIVATION INHIBITOR of key genes involved in cancer
- APOPTOSIS induced at very low concentrations

Yondelis™: Facts and Figures

- Broad Joint Development Plan with J&J (Ortho Biotech)
- Common registration strategy for US and EU
- Orphan Drug designation in EU for Soft Tissue Sarcoma (2001) and Ovarian cancer (2003)
- More than 2,200 patients treated in over 50 hospitals in EU and US
- Over 750 patients treated on compassionate use for Soft Tissue Sarcoma
- Negative opinion from CPMP for marketing authorization in STS in November 03

CPMP – Methodological Issues

THREE PROSPECTIVE PHASE 2 TRIALS IN PRETREATED ADVANCED OR METASTATIC STS EVALUATING YONDELIS™ 1.5 mg/m² q3w (24h ci)

STANDARD PHASE II DESIGN

INCLUSION CRITERIA: PROGRESSIVE DISEASE TO PRIOR THERAPY

END-POINTS: PRIMARY: RR SECONDARY: TTP, OS, TOXICITY

183 PATIENTS (most extensively studied "third" drug in STS)

PUT INTO CLINICAL CONTEXT

EORTC data base

↓

BEST- ONLY CHOICE

ANALYSIS

SUB-GROUP WITH STS RESISTANT TO ANTHRACYCLINES AND IFOSFAMIDE

63 PATIENTS

- Following CPMP recommendation
- Largest set of data available in a strictly defined group of double resistant STS

CPMP Grounds for Refusal - Methodology

*"The **sub-population for the efficacy evaluation and historical control were identified retrospectively**; the absence of pre-specification as regards key measures and comparisons violates fundamental methodological principles and may introduce bias in the assessment of benefit/risk balance"*

*"The wide confidence intervals around the point estimates for RR and PFS at 6 months, the trends towards even lower anti-tumour activity in the French ATU programme and the possibility of non-representativeness of patients included in the retrospective evaluation of efficacy, altogether **seriously question the possibility to estimate with reasonable certainty the anti-tumour activity** of trabectedin for patients in clinical practice"*

*"Time to progression (TTP) on last prior therapy before inclusion in the trabectedin studies was found to be twice as long as TTP on trabectedin therapy. In contrast, PFS on trabectedin was found to be very similar to PFS on ifosfamide second-line in the historical comparison. Despite similarity in PFS in the historical comparison overall survival appeared to favour trabectedin at late time points. Altogether these partly contradictory findings indicate that the **historical comparison with ifosfamide is hampered by bias**"*

PHARMAMAR´S APPEAL POINT PER POINT

Rapporteur / Co-rapporteur Assessment

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" In appealing against the CPMP's grounds for refusal of the marketing authorisation I believe that the Applicant has resolved most of the issues which are capable of resolution. Methodological problems relating to the sub-population selection and confidence intervals have been resolved, and an apparent discrepancy between progression free and overall survival has been plausibly explained."

" It is agreed that the use of phase II clinical trials is an appropriate and adequate means to investigate anticancer medicinal products in patient populations who have exhausted all other treatment options. The double-resistant STS patients are a relevant target for experimental treatment with trabectedin. The unwillingness of patients and doctors to randomise to best supportive care is fully recognised and accepted."

" The new analyses and the arguments provided by the company support the claim that no serious bias has been introduced and that there are no obvious evidence of contradictions in the TTP, PFS and overall survival data both within the trabectedin group and in the comparison of trabectedin with the ifosfamide reference group."

"The Applicant provides a robust response on this issue indicating that important inclusion / exclusion criteria, were in fact prospectively defined and were applied by experts independent of the applicant to select a historic control population."

"The Applicant's response is considered to meet CPMP's objection."

Rapporteur / Co-rapporteur Assessment

" The requirement in the CPMP anti-cancer Note for Guidance to demonstrate outstanding anti-tumour activity if approval is to be based on non-randomised study data only is, therefore, the single most important regulatory issue for this application..... Unfortunately, there is no definition of what is meant by outstanding."

POOL ANALYSIS DATA OF THREE PROSPECTIVE RANDOMIZED TRIALS IN PRE-TREATED STS

NO METHODOLOGICAL ISSUES IN THE DESIGN, CONDUCT OR ANALYSIS OF THESE TRIALS

METHODOLOGICAL LIMITATIONS ARISE ON HOW TO INTERPRET DATA FROM NON-RANDOMIZED STUDIES AND HOW TO QUALIFY IT AS OUTSTANDING

Yondelis™ Activity in Double Resistant STS

Pharma Mar

RESPONSE	Double resistant patients (n=63)
Partial response (PR) Median duration (range) Responses with duration > 6 months Responses with duration > 12 months	**10% (4-20)** 11.4 months (4-17) 83% 50%
Minor objective response* (MR) (Tumor shrinkage range from 29 to 47%)	**6% (2-15)**
Stable disease (SD)	**27% (17-40)**
Tumour growth control (PR+MR+SD)	**43% (31-56)**
Progressive disease (PD)	**56% (42-68)**

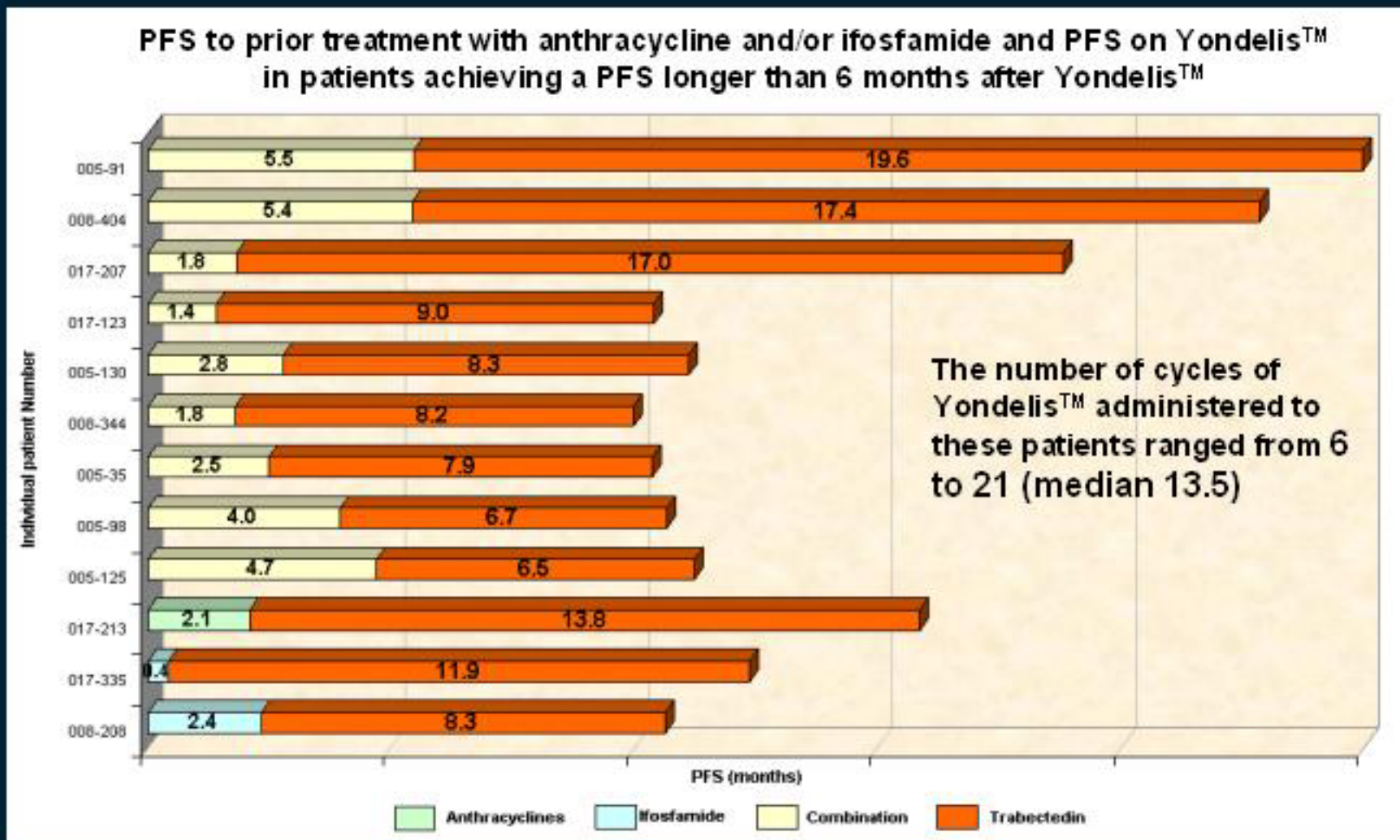
In progressing double resistant STS trabectedin induces:

- long lasting responses
- high rate of tumour growth control
- a lower PD rate than other salvage treatments

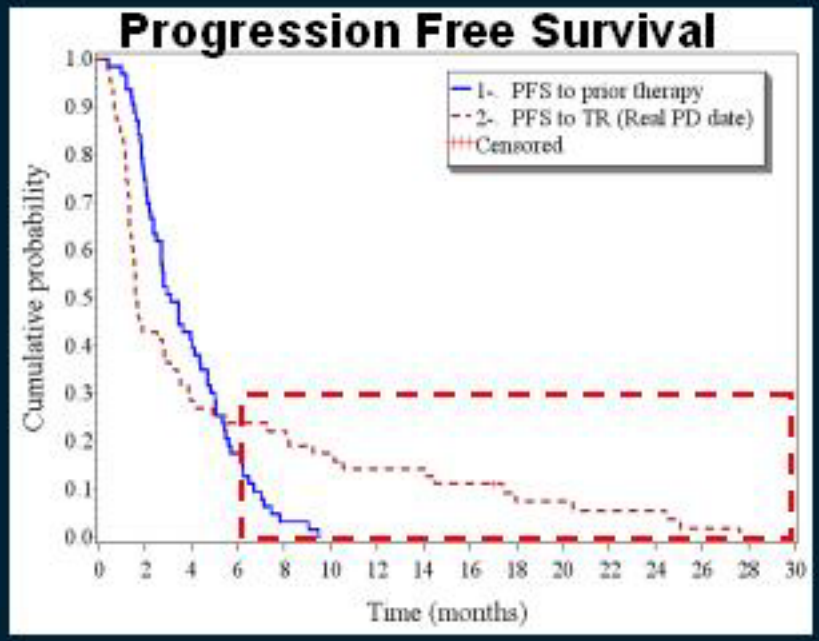
Yondelis™ – STS Responders

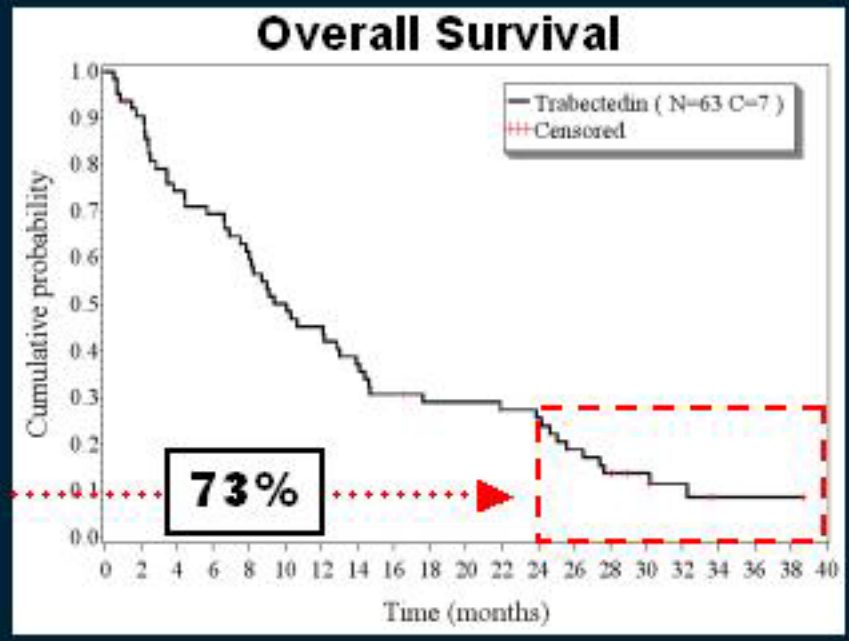
In double resistant and rapidly progressive STS:

- **Yondelis™ causes outstanding PFS duration in a clinically meaningful rate of these patients**
- **The achievement of such a long lasting PFS is an effect unequivocally due to Yondelis™**



Yondelis™ – STS Survival





- Yondelis™ changes the natural history in a clinically meaningful proportion (PFS at 6 months of 22%) of double resistant and rapidly progressing STS by inducing outstanding duration of PFS
- This beneficial effect of Yondelis™ may be related to prolonged administration due to good subjective tolerance and lack of cumulative toxicities
- The beneficial impact of Yondelis™ on PFS translates into long survival in the majority of these patients

Yondelis™ – STS Conclusions

The data discussed support that the anti-cancer activity of trabectedin in double resistant and progressive STS should be considered outstanding:

- response rate (10%)
- proportion of patients with PFS at 6 months (22%)
- remarkable long duration of PFS
- long term survival (25% at 24 months)
- favourable safety profile allowing prolonged administration in the absence of PD

These results demonstrate that Yondelis™ is the only treatment option for double resistant patients thus fulfilling an unmet medical need

Yondelis™

Clinical Development Plan

Yondelis™ – Phase II Trials

TUMOUR TYPE	LINE	END-POINT	1st PATIENT	TARGET PTS	STATUS
STS	2nd-3rd • Randomized between 2 Yondelis schedules	RR	May-03	130/arm	Ongoing
OVARIAN	2nd-3rd	RR	Jun-00	59	Completed
OVARIAN	2nd-3rd • Platinum sensitive • Randomized between 2 Yondelis schedules	RR	Dec-03	100	Ongoing
OVARIAN	2nd-3rd	RR	Oct-02	100	Ongoing
ENDOMETRIUM	2nd	RR	April-02	100	Ongoing
PROSTATE	2nd	RR	Jan-04	33	Ongoing
BREAST	3rd • Randomized between 2 Yondelis schedules	RR	Nov-02	45/arm	Ongoing
NSCLC	1st-2nd	RR	0ct-01	64	Analysis
PAEDIATRIC TUMOURS	1st-2nd	RR	2005	56	Planned

Yondelis™ – Phase I Combination Trials

Combinations increase the potential of Yondelis™ for the treatment of a broader spectrum of solid tumours

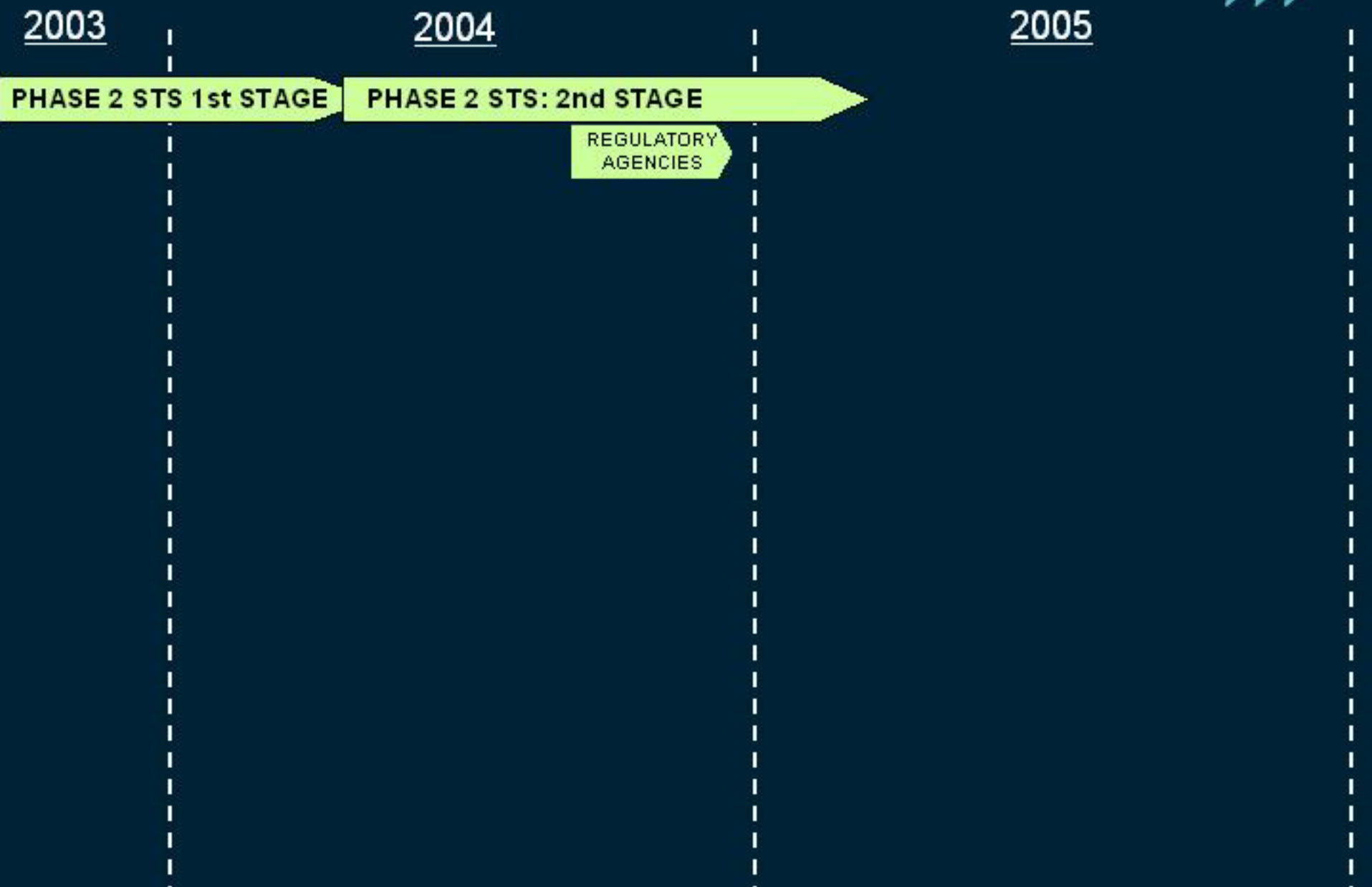
COMBINATION	TUMOUR TYPE	ENDPOINT	TARGET PTS	1ST PATIENT	STATUS
YONDELIS (d1) + DOXORUBICIN (d1)	• STS, Breast • Expanded cohort STS, breast	• MTD, DLT • RR in 1st line STS and breast	50	June 01	Recruitment at expanded cohort
YONDELIS (d1,8) + DOXORUBICIN (d1)	Solid tumours (Gynecoloc, breast, STS)	MTD,DLT	36	Sep 03	Ongoing
YONDELIS (d1,8) + DOXIL® (d1)	Solid tumours	MTD, DLT	34	Oct 02	Ongoing
YONDELIS (d1,8) + CISPLATIN (d1,8)	• Solid tumours • Expanded cohort NSCLC	MTD, DLT RR in 1 st line NSCLC	76	Feb 02	Recruitment at expanded cohort
YONDELIS (d1) + CARBOPLATIN (d1)	Solid tumours	MTD, DLT	30	June 03	Ongoing
YONDELIS (d1,15) + PACLITAXEL (d1,15)	Solid tumours	MTD, DLT	30	Aug 02	Ongoing
YONDELIS (d1) + DOCETAXEL (d1)	Solid tumours	MTD, DLT	30	June 02	Ongoing
YONDELIS (d1,15) + GEMCITABINE	Solid tumours	MTD, DLT	36	March 03	Ongoing
YONDELIS (d1,15) + CAPECITABINE	Solid tumours	MTD, DLT	36	Oct 02	Ongoing

Yondelis™ – Soft Tissue Sarcoma

TUMOUR TYPE/DESIGN	LINE	LOCATION /CENTERS	END-POINT	TARGET PTS	1ST PATIENT
STS Randomized between 2 Yondelis schedules	3rd	USA, EU, Australia, Canada, Russia 46	Clinical benefit	130/arm	May 03

- Study sponsored by J&J within the JDP
- Recruitment exceeding schedule
- Single agent registration strategy
- Scientific advice from regulatory agencies

Yondelis™ Clinical Dev. Plan Chart (1)



Yondelis™ – Ovarian Cancer

Pharma Mar

Very promising activity in platinum sensitive, relapsed ovarian cancer

TUMOUR TYPE/DESIGN	LINE	LOCATION / CENTERS	END-POINT	TARGET PTS	1ST PATIENT	STATUS
OVARIAN CANCER	2nd-3rd	EU	RR	50 evaluable	Jun 00	Completed

RESPONSE RATE (PEER REVIEW)

	PATIENTS EVALUABLE	CR+PR	SD	PD
SENSITIVE	24	46%	33%	17%
RESISTANT	26	4%	15%	81%
TOTAL	50	24%	11%	15%

OVARIAN CANCER • Platinum sensitive • Randomized between 2 Yondelis schedules	2nd-3rd	EU 38	RR	100	Dec 03	Ongoing
OVARIAN CANCER	2nd-3rd		RR	100	Oct 02	Ongoing

Yondelis™ – Ovarian Cancer Combinations

Pharma Mar

PHASE 1 TRIALS

COMBINATION	TUMOUR TYPE	ENDPOINT	TARGET PTS	STATUS
YONDELIS (d1,8) + DOXIL® (d1)	Solid tumours	MTD, DLT	34	Ongoing
YONDELIS (d1,8) + CISPLATIN (d1,8)	• Solid tumours • Expanded cohort NSCLC	• MTD, DLT • RR in 1 st line NSCLC	55	Recruitment at expanded cohort
YONDELIS (d1) + CARBOPLATIN (d1)	Solid tumours	MTD, DLT	30	Ongoing

PLATINUM-SENSITIVE RELAPSED OVARIAN CANCER

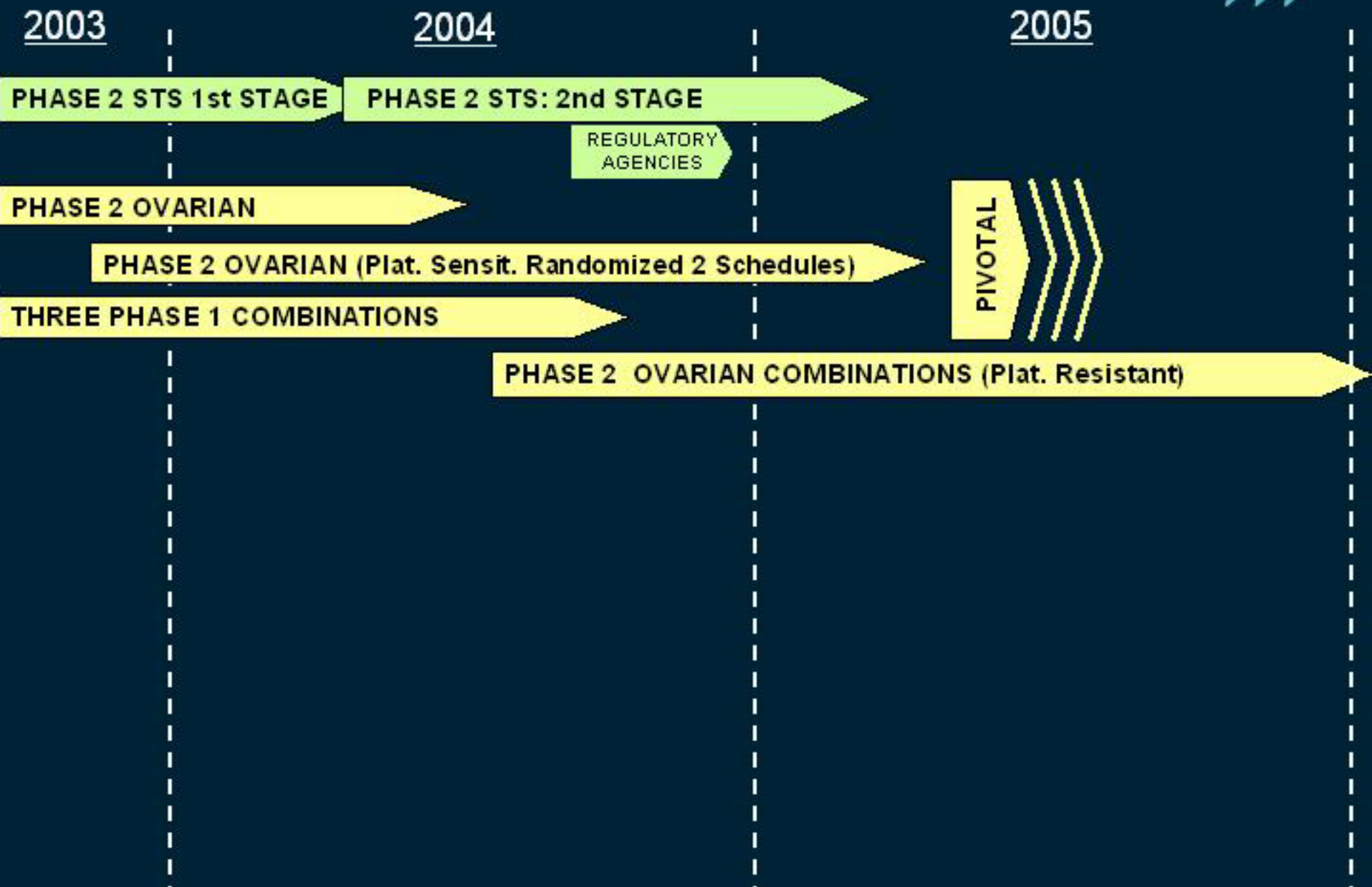
- ICON-4 results indicate potential changes in standard of care
- Combinations may play a major role

PLATINUM-RESISTANT RELAPSED OVARIAN CANCER

- Difficult-to-treat population
- Lack of truly active single agents

DATA DRIVEN DEVELOPMENT STRATEGY

Yondelis™ Clinical Dev. Plan Chart (2)



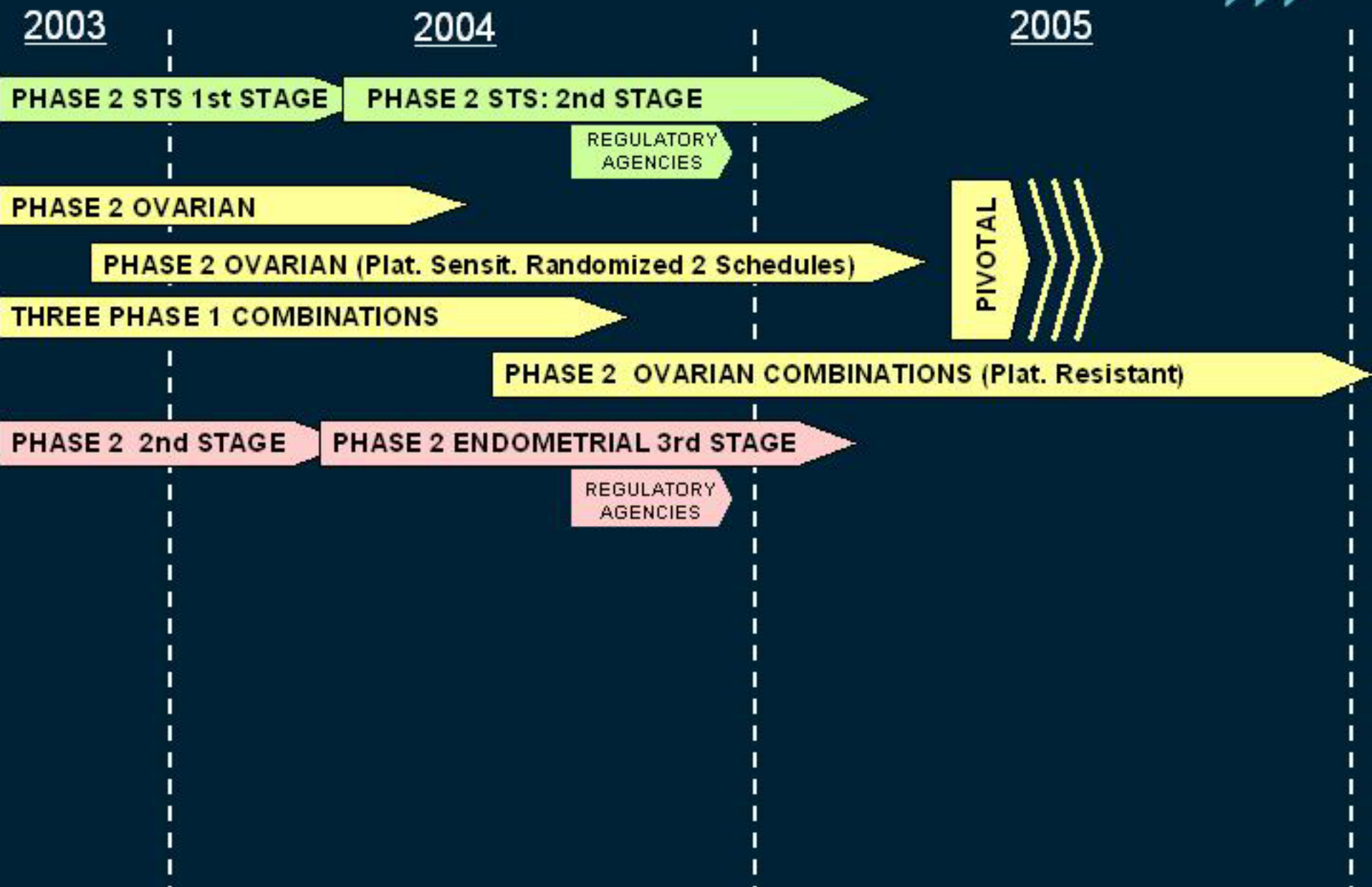
Yondelis™ – Endometrial Carcinoma

SINGLE AGENT STUDY

TUMOUR TYPE	LINE	LOCATION /CENTERS	END-POINT	TARGET PTS	1ST PATIENT	STATUS
Endometrial cancer	2nd	USA, EU, Canada, Russia 33	RR	100	April 02	Ongoing

- Study sponsored by J&J within the JDP
- Recruitment exceeding schedule
- Planned discussions with EU and US Regulatory Agencies

Yondelis™ Clinical Dev. Plan Chart (3)



Yondelis™ – Breast Cancer

SINGLE AGENT STUDY

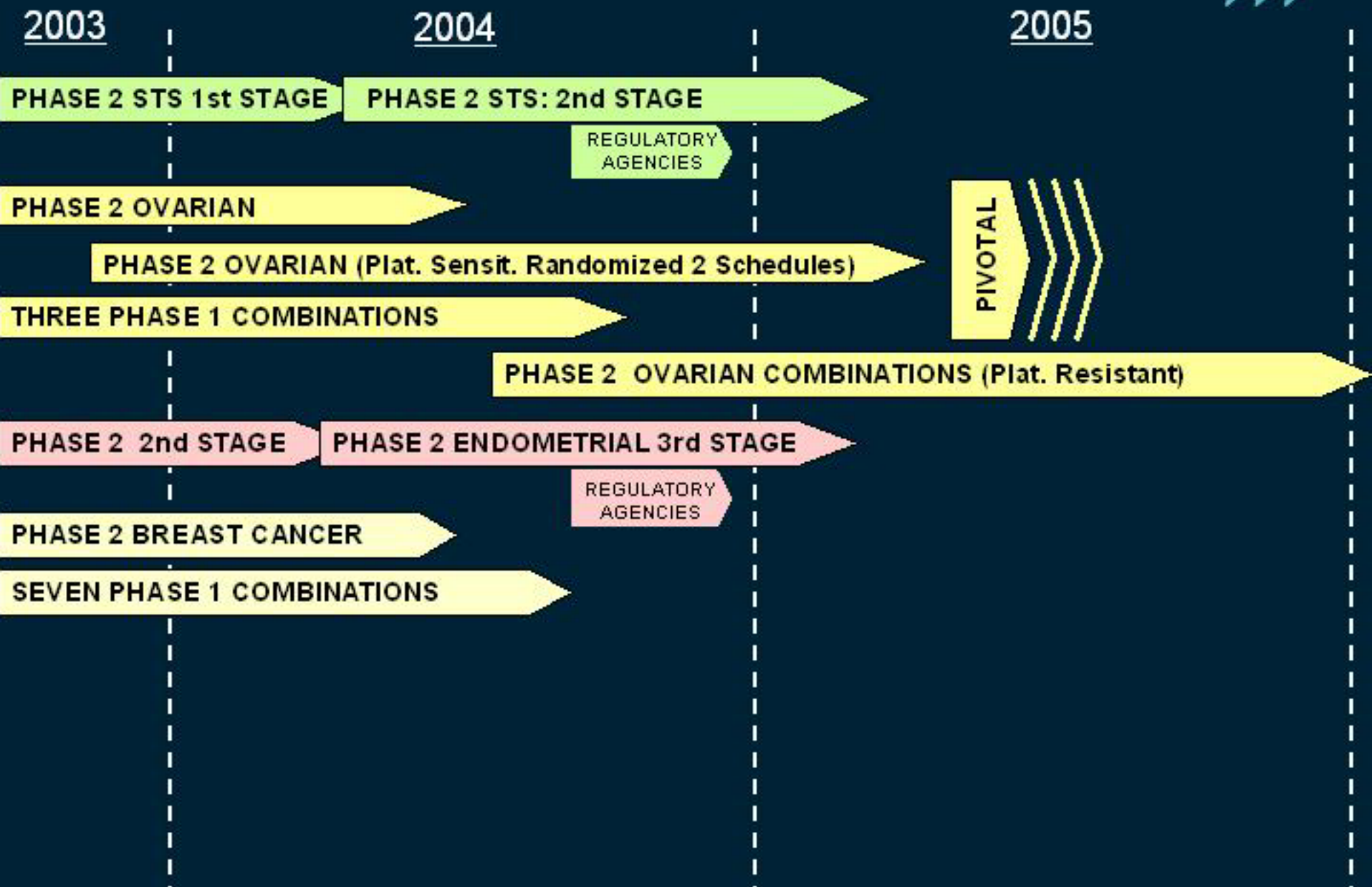
TUMOUR TYPE / DESIGN	LINE	LOCATION /CENTERS	END-POINT	TARGET PTS	1ST PATIENT
• Breast cancer • Randomized between 2 Yondelis schedules	3rd	USA, EU, Canada, Russia, Israel 24	RR	45 / arm	Nov 02

PHASE 1 TRIAL COMBINATIONS WITH YONDELIS RELEVANT TO BREAST CANCER

- YONDELIS (d1) + DOXORUBICIN (d1)
  EXPANDED COHORT IN STS AND BREAST
- YONDELIS (d1,8) + DOXORUBICIN (d1)
- YONDELIS (d1,8) + DOXIL® (d1)
- YONDELIS (d1,15) + PACLITAXEL (d1,15)
- YONDELIS (d1) + DOCETAXEL (d1)
- YONDELIS (d1,15) + GEMCITABINE
- YONDELIS (d1,15) + CAPECITABINE

FURTHER DEVELOPMENT STRATEGY WILL BE DATA DRIVEN AFTER SINGLE AND COMBINATION STUDIES PROVIDE SUFFICIENT DATA

Yondelis™ Clinical Dev. Plan Chart (4)



Yondelis™ – NSCLC

SINGLE AGENT STUDY

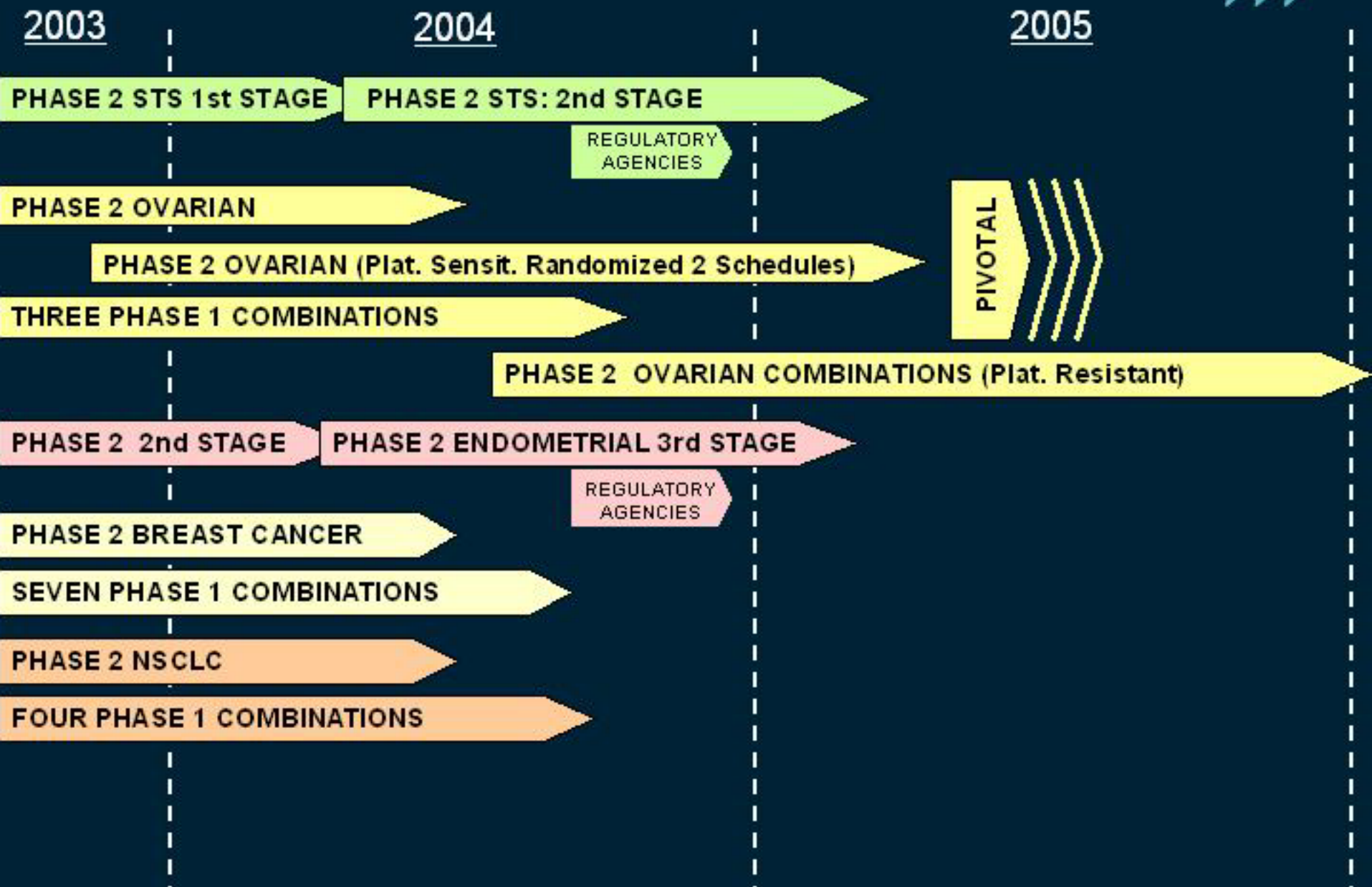
TUMOUR TYPE / DESIGN	LINE	LOCATION /CENTERS	END-POINT	TARGET PTS	1ST PATIENT
NSCLC	1st-2nd	EU 6	RR	• 1st 32 • 2nd 32	Oct 01

PHASE 1 TRIAL COMBINATIONS WITH YONDELIS RELEVANT TO LUNG CANCER

- YONDELIS (d1,8) + CISPLATIN (d1,8)
  - EXPANDED COHORT IN NSCLC ONGOING
- YONDELIS (d1) + CARBOPLATIN (d1)
- YONDELIS (d1,15) + PACLITAXEL (d1,15)
- YONDELIS (d1) + DOCETAXEL (d1)

FURTHER DEVELOPMENT STRATEGY WILL BE DATA DRIVEN AFTER SINGLE AND COMBINATION STUDIES PROVIDE SUFFICIENT DATA

Yondelis™ Clinical Dev. Plan Chart (5)



Yondelis™ – Prostate Cancer

SINGLE AGENT STUDY

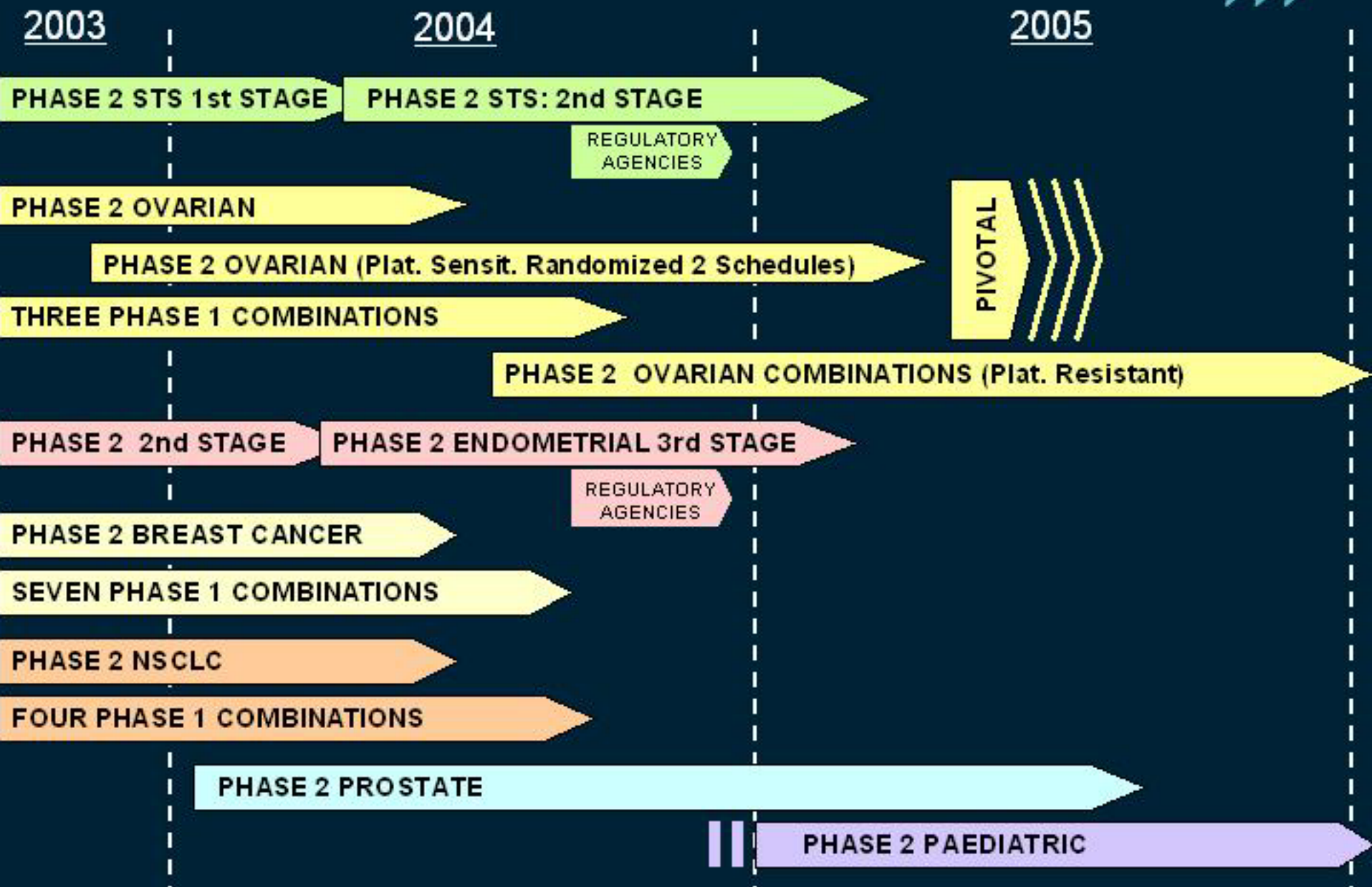
TUMOUR TYPE / DESIGN	LINE	LOCATION /CENTERS	END-POINT	TARGET PTS	1ST PATIENT	STATUS
Prostate	2nd	USA 1 (MSKCC)	RR	33	Jan 04	Ongoing

Yondelis™ – Paediatric Cancer

SINGLE AGENT STUDY

TUMOUR TYPE / DESIGN	LINE	LOCATION /CENTERS	END-POINT	TARGET PTS	1ST PATIENT	STATUS
Ewing Sarcoma Soft Tissue Sarcoma Neuroblastoma Rhabdomyosarcoma	2nd	USA Canada	RR	56	Jan 05	-

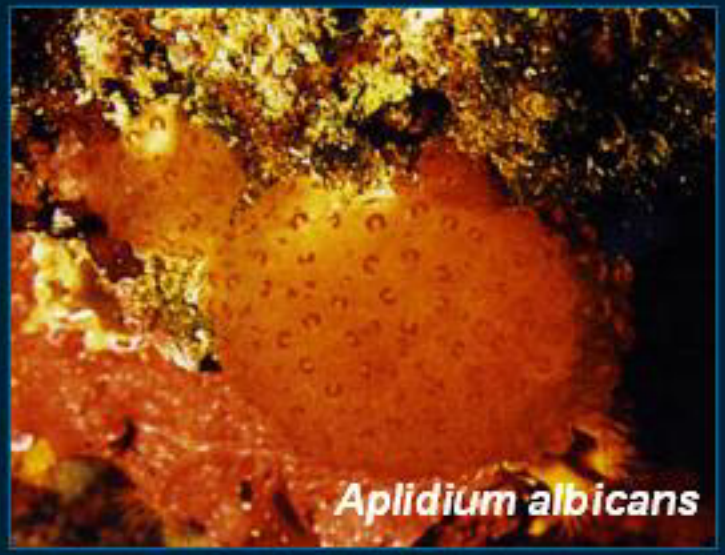
Yondelis™ Clinical Dev. Plan Chart (6)

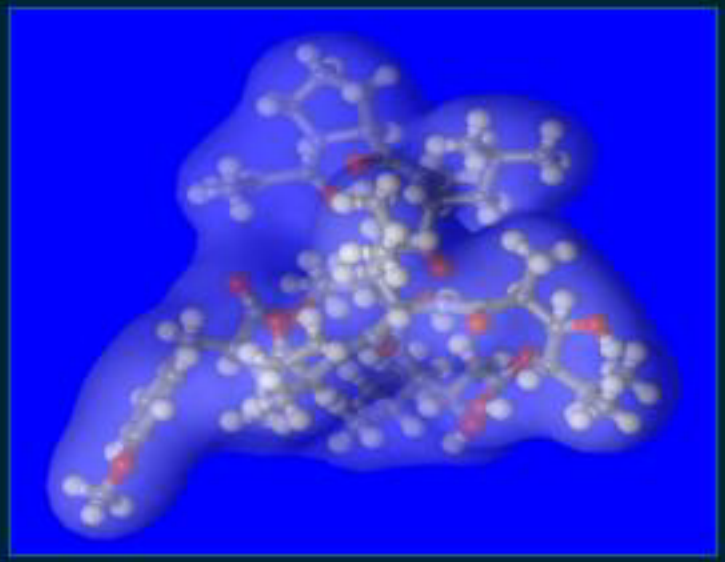


Aplidin®

Clinical Development Plan

Aplidin® – Structure & Mode of Action





UNIQUE INDUCTION OF APOPTOSIS

- Very potent and rapid
- Fast and sustained JNK activation
- p53 independent
- No DNA or microtubules interaction

BLOCK OF CELL CYCLE

- Blocks cell cycle in G1/S

ANTI-ANGIOGENIC

- Blocks VEGF autocrine loop

Aplidin® Phase I Trials

- GOOD SAFETY PROFILE:
  - Manageable and Transient Adverse Effects
  - Suitable for combination therapy
- CLINICAL BENEFIT IN A BROAD SPECTRUM OF TUMOUR TYPES

SAFETY

- Low incidence of severe toxicities at the RD
- More frequent toxicities include:
  - ALT/AST increase: mild, reversible, non-cumulative
  - Asthenia
  - Mild muscular toxicity (pain, weakness, CPK increase)
- Low incidence of:
  - Non-controlled nausea and vomiting
  - Diarrhoea
  - Mucositis
  - Alopecia
- Absence of clinically relevant haematological toxicity

CLINICAL BENEFIT AS PER INVESTIGATOR

- Renal Carcinoma
- GI tumours
- Head and Neck tumours
- Medullary Thyroid carcinoma
- Lung cancer
- Non-Hodgkin Lymphoma
- Melanoma
- Sarcoma

215 PATIENTS TREATED

Aplidin® - Responses

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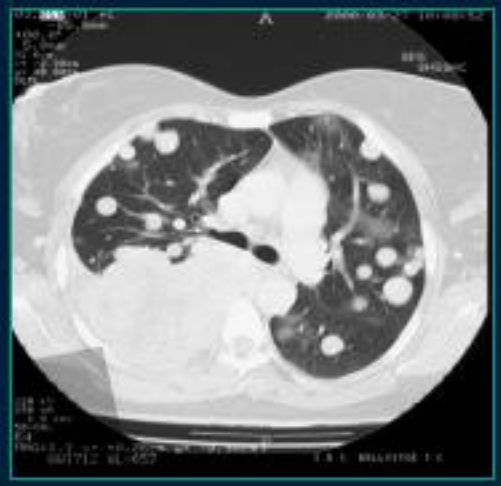
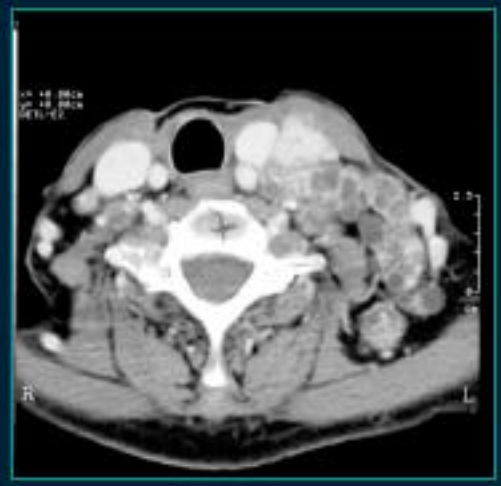
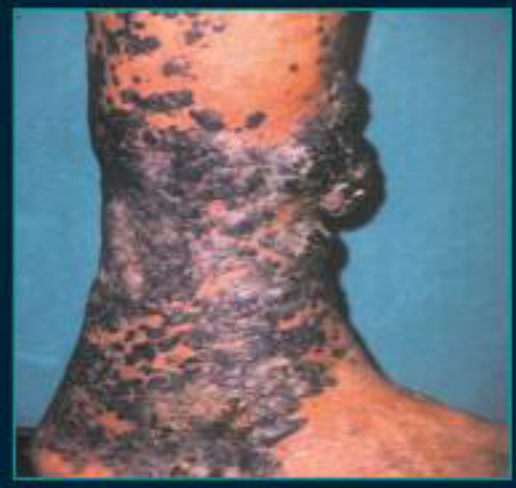
BEFORE APLIDIN

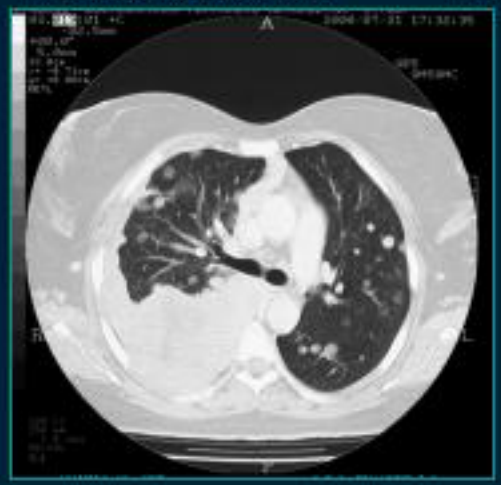


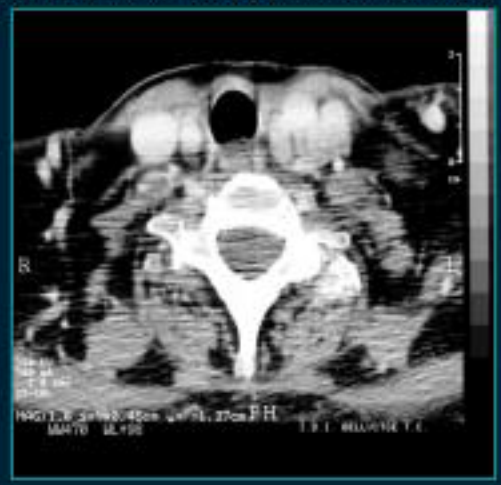


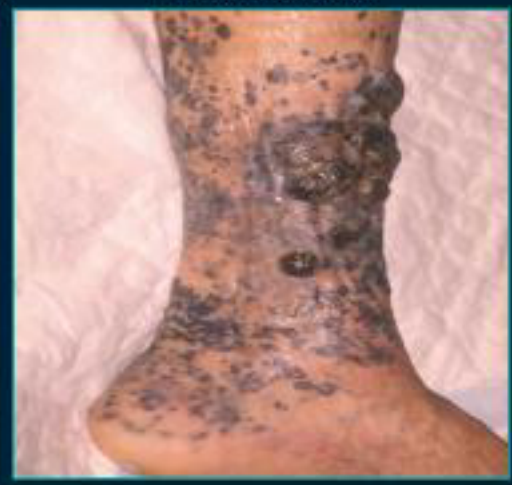


RENAL CANCER **MEDULLARY THYROID CANCER** **MELANOMA**

AFTER APLIDIN







Aplidin® - Clinical Development Plan

1. SOLID TUMOURS: PHASE 2

Colon	Head & Neck
Renal	NSCLC
MTC	SCLC
Melanoma	Bladder
Pancreas	Prostate

2. HAEMATOLOGICAL MALIGNANCIES: PHASE 2

Multiple Myeloma

Acute Leukaemia

Indolent Non-Hodgkin Lymphomas

Aggressive Non-Hodgkin Lymphomas

3. PAEDIATRIC TUMOURS: PHASE 1

Solid tumours

Haematological malignancies

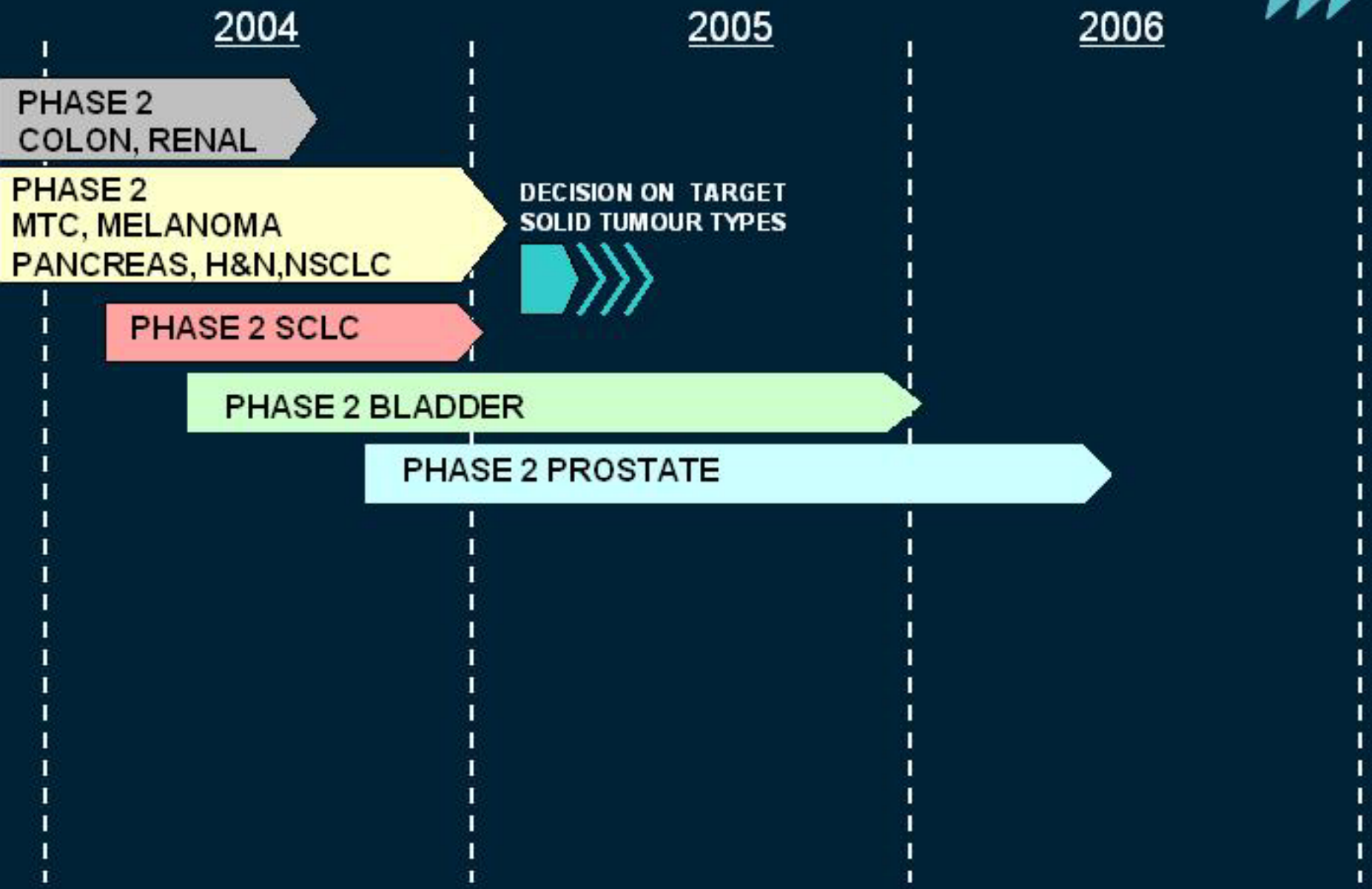
Aplidin® - Solid Tumours

Pharma Mar

STATUS OF PHASE 2 TRIALS

TUMOUR TYPE	LINE	LOCATION / CENTERS	END-POINT	1st PATIENT	TARGET PATIENTS	STATUS
Colon	3rd	EU / 8	RR	Dec. 01	38	Ongoing
Renal	2nd	EU / 8	RR	Oct. 01	38	Ongoing
MTC	2nd	EU / 8	RR	Feb. 03	15/ 25	Ongoing
Melanoma	2nd / 3rd	EU, Canada / 5	RR	Sep. 03	18 / 32	Ongoing
Pancreas	1st	EU / 3	RR	June 03	18 / 32	Ongoing
Head & Neck	2nd / 3rd	EU / 4	RR	June 03	18 / 32	Ongoing
NSCLC	2nd / 3rd	EU / 6	RR	June 03	17 / 37	Ongoing
SCLC	2nd	EU, Canada / 4	RR	Q1 04	18 / 32	IRB submitted
Bladder	2nd	EU / 5	RR	Q2 04	18 / 32	Submission Q1 04
Prostate	2nd	US / 1	RR	Q3 04	18 / 32	Planned

Aplidin® - Clinical Dev. Plan Chart (1)



Aplidin® - Haematological Malignancies

- **Strong preclinical rationale to initiate clinical development of Aplidin® in different haematological malignancies**

  Multiple Myeloma

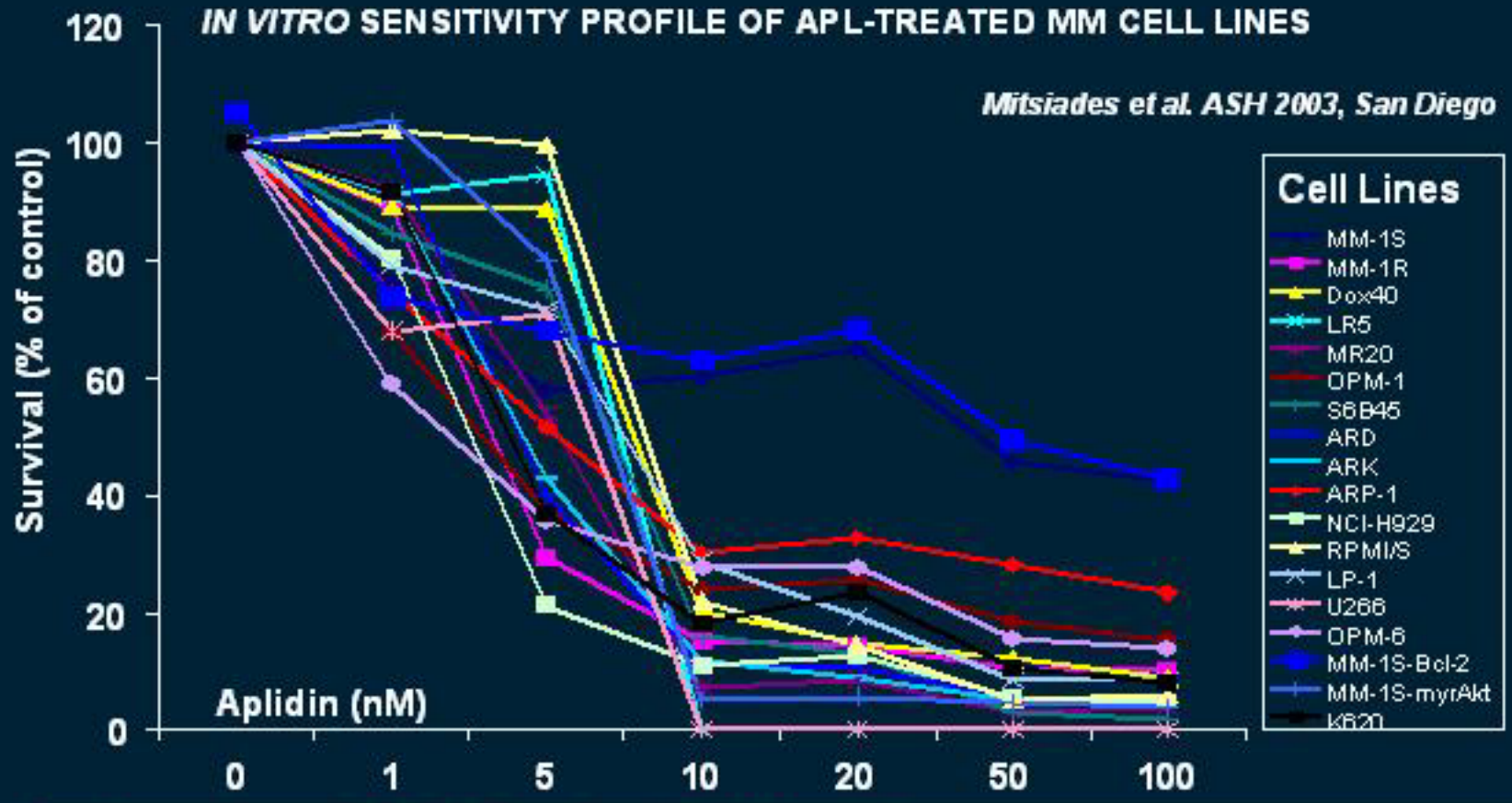
  Acute Lymphoblastic Leukaemia (ALL)

  Low Grade Non-Hodgkin Lymphomas

  High Grade Non-Hodgkin Lymphomas

- **Compelling safety data from Phase I data**
- **Orphan drug designation by COMP-EMEA (November 2003) for ALL**

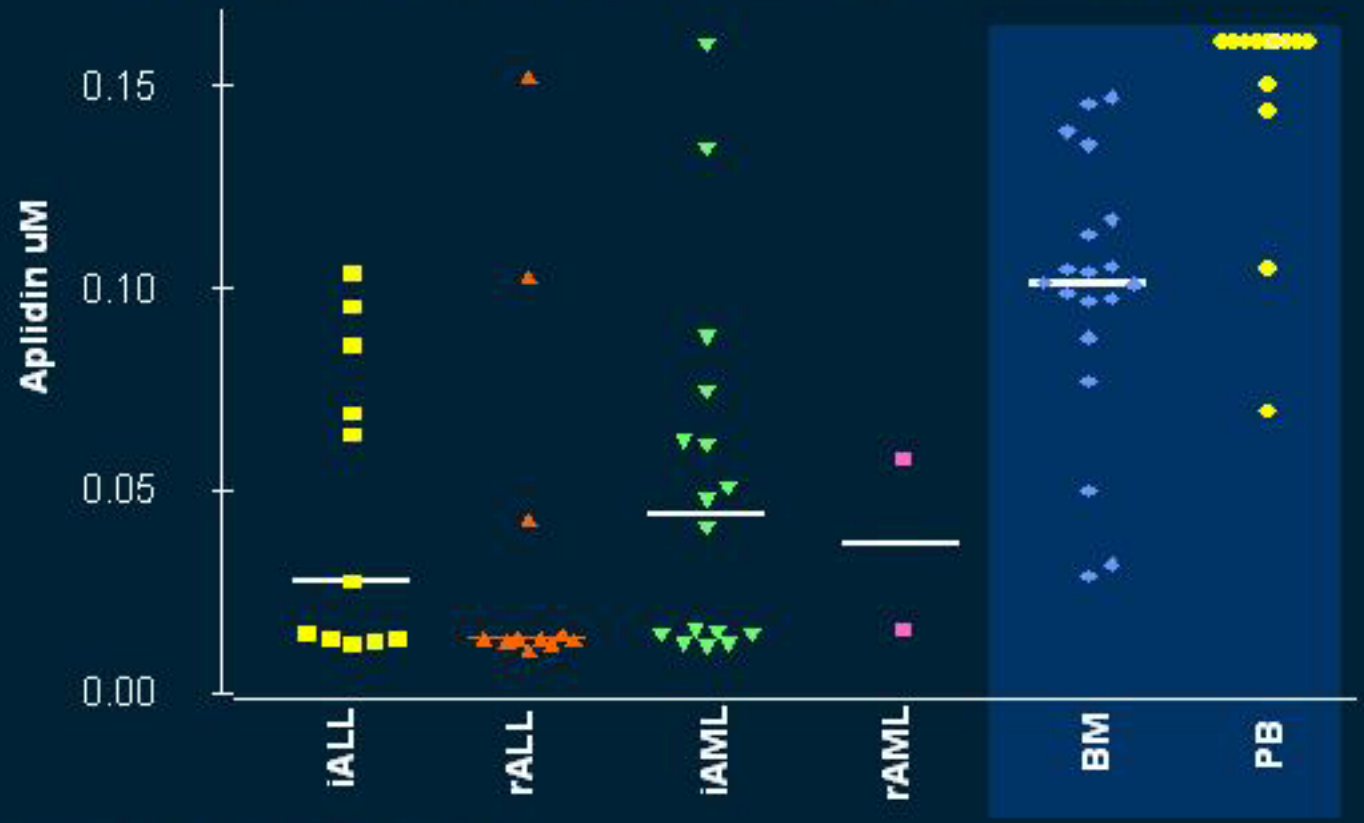
Aplidin® - Activity in Multiple Myeloma



- IC_{50} values : <10 nM for almost all MM cell lines
- No association of the degree of Aplidin-sensitivity with status of resistance to conventional or novel agents with anti-MM activity
- Overexpression of anti-apoptotic molecules did not preclude sensitivity to Aplidin

Aplidin® - Activity in Leukaemia

Samples of different subgroups of leukaemias (iALL, rALL, iAML, rAML) and normal blood cells (BM, PB). Aplidin® LC75 data



Bresters et al. BJC 17: 1388, 2003

Aplidin® shows selective cytotoxicity against different subgroups of leukaemia versus normal blood cells

Aplidin® - Activity in Leukaemia

Pharma Mar

Cross-resistance of Aplidin with other cytotoxic drugs in 40 leukaemia samples

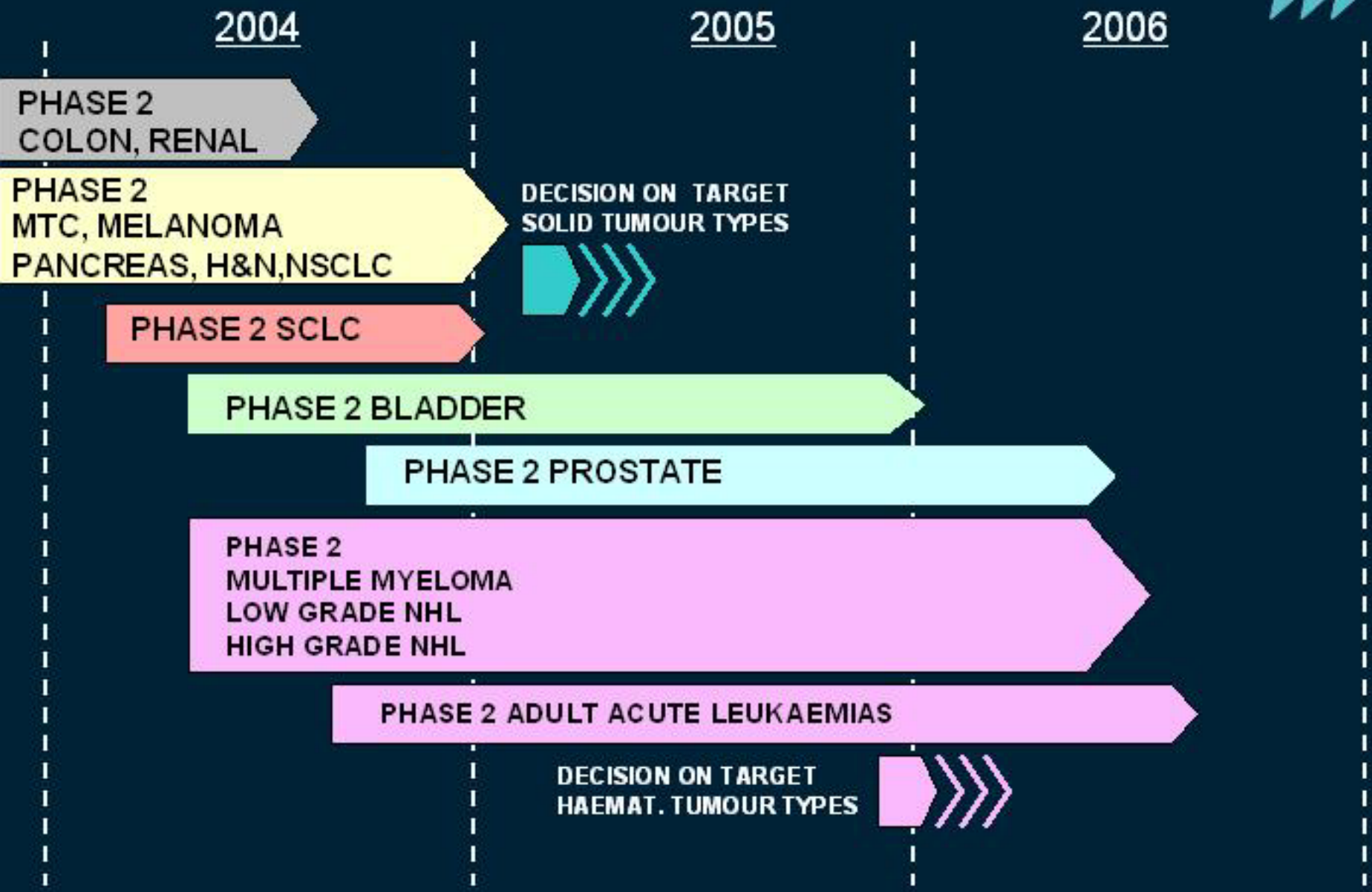
LC75 Compound	Rho (1)	P (2)	N (3)	LC75 Compound	Rho (1)	P (2)	N (3)
AMSA	0,228	ns	18	FLU	0,442	ns	10
ARA-C	0,055	ns	36	**GEM**	**0,727**	**0.011**	**11**
AZA	-0,224	ns	16	IDA	0,357	ns	23
L-ASP	-0,059	ns	36	IFOS	0,152	ns	30
BUS	0,029	ns	18	MITOX	0,276	ns	27
CDA	0,074	ns	33	6MP	0,079	ns	16
DEX	-0,216	ns	20	PRED	0,002	ns	35
DNR	0,137	ns	40	TENI	0,308	ns	12
DOX	0,272	ns	22	6TG	0,135	ns	36
ETO	0,19	ns	34	VCR	0,176	ns	36

1/ rho = correlation coefficient.
2/ p value for statistical significance, ns = not significant (i.e. p>0.05).
3/ n = number of samples tested.

G. Kaspers et al Procc AACR 2002

Aplidin® does not show cross-resistance with established anti-leukaemic cytotoxic drugs

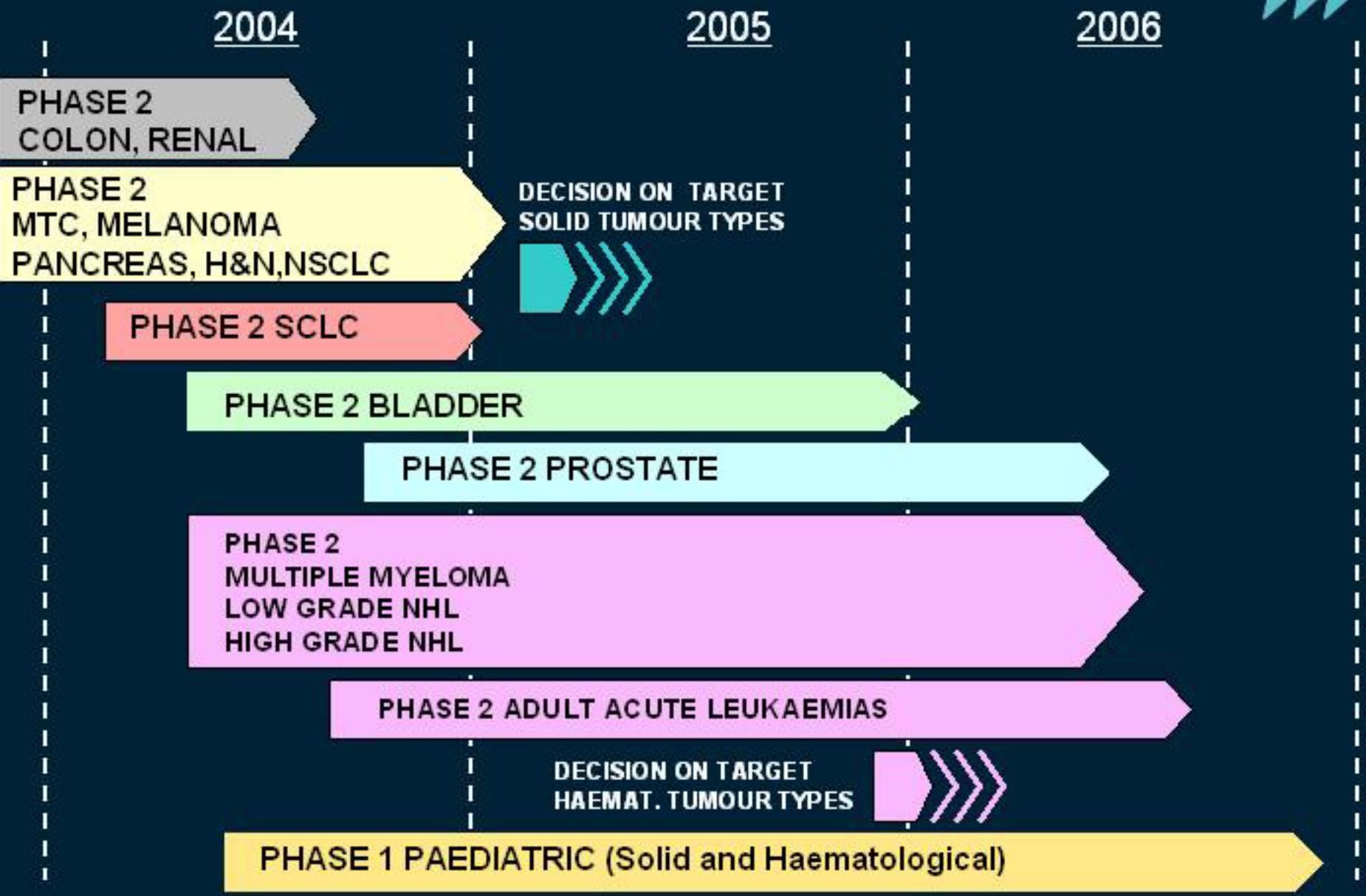
Aplidin® - Clinical Dev. Plan Chart (2)



Aplidin® - Phase I Paediatric Tumours

TUMOUR TYPE / DESIGN	LINE	LOCATION /CENTERS	END-POINT	TARGET PTS	1ST PATIENT	STATUS
• Solid tumours • Expanded cohort at the RD in solid tumours and acute leukaemias	Pretreated patients	• EU • 4	MTD	41	March 04	IRB approved

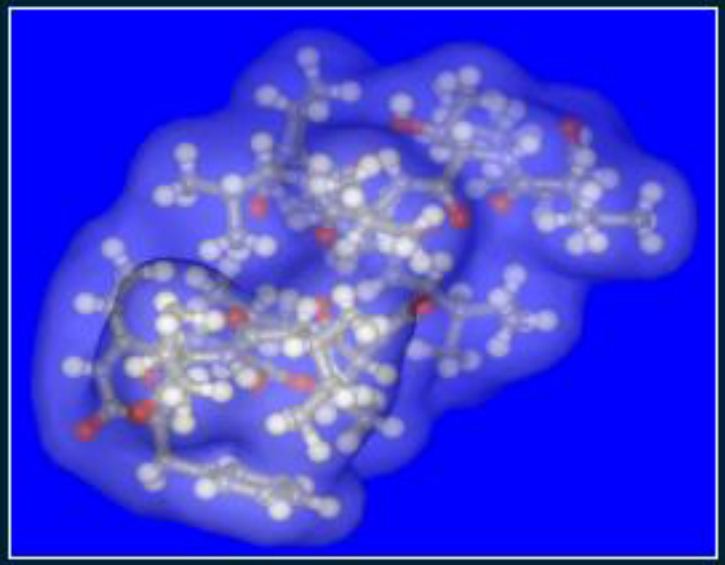
Aplidin® - Clinical Dev. Plan Chart (3)



Kahalalide F (K-F)

Clinical Development Plan

Kahalalide F – Structure & Mode of Action



- Destabilizes lysosomal and ER membranes
- Inhibits TGF-alpha expression
- Blocks signalling downstream of EGF and ErbB2 receptor family
- Induces non-p53 mediated apoptosis
- MDR expression independent
- NCI-COMPARE negative

Kahalalide F – Phase I

SCHEDULE	TUMOUR TYPE	PATIENTS	DLT	RD	CLINICAL ACTIVITY
1 h/d x 5 3 weeks	Prostate Cancer (adva. / metast.)	32	Elevation AST / ALT	560 $\mu g/m^2$	YES
1 h/d weekly	Solid tumours	38	Elevation AST / ALT	650 $\mu g/m^2$	YES

Kahalalide F – Phase I Trials

- EXCEPTIONAL SAFETY PROFILE FOR ANTI-CANCER DRUG
- CLINICAL BENEFIT IN A BROAD SPECTRUM OF TUMOUR TYPES

SAFETY

- Low incidence of severe toxicities at the RD
- More frequent toxicities include:
  - ALT/AST increase: mild, reversible, non-cumulative,
  - Tingling or pricking palms
- Absence of clinically relevant:
  - Nausea and vomiting
  - Diarrhoea
  - Mucositis
  - Alopecia
  - Haematological toxicity
- Weekly treatment can be safely given for up to 20 months

CLINICAL BENEFIT AS PER INVESTIGATOR

- Hepatocarcinoma
- Melanoma
- NSCLC
- Pancreatic cancer
- Mesothelioma
- Cavum carcinoma

70 PATIENTS TREATED

Kahalalide F – Clinical Plan

STUDY TYPE	TUMOUR TYPE	LOCATION CENTERS		TARGET PATIENTS	1ST PATIENT	STATUS
Phase 1 Protracted infusion	Solid tumours	EU	3	30	Aug 03	Ongoing
Phase 2	Hepatocarcinoma	EU	5	19 / 40	June 03	Ongoing
Phase 2	NSCLC	EU	TBD	TBD	2Q 04	Planned
Phase 2	Melanoma	EU	TBD	TBD	2Q 04	Planned

Kahalalide F – Clinical Plan

STUDY TYPE	TUMOUR TYPE	LOCATION CENTERS		TARGET PATIENTS	1ST PATIENT	STATUS
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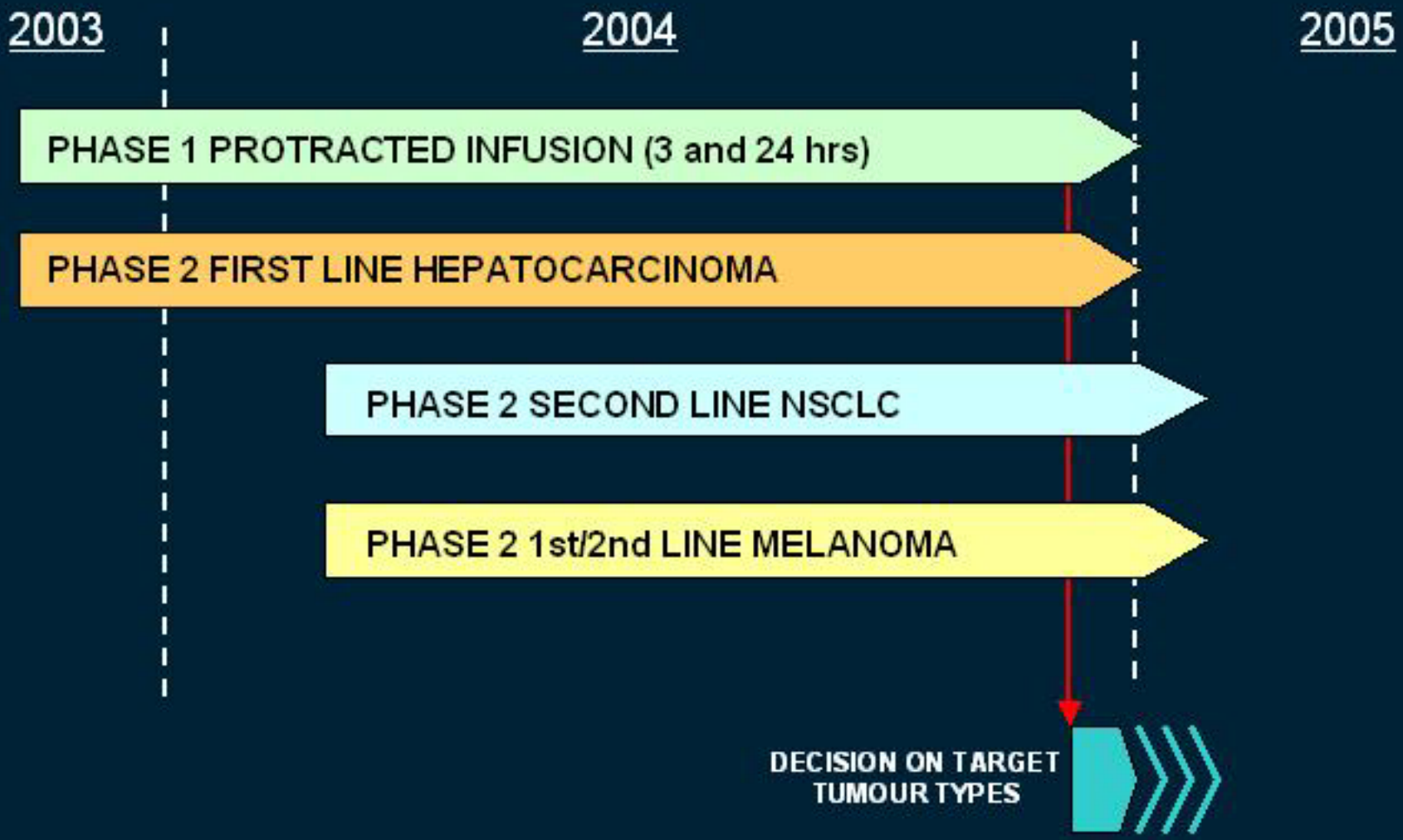
Kahalalide F – Clinical Dev. Plan

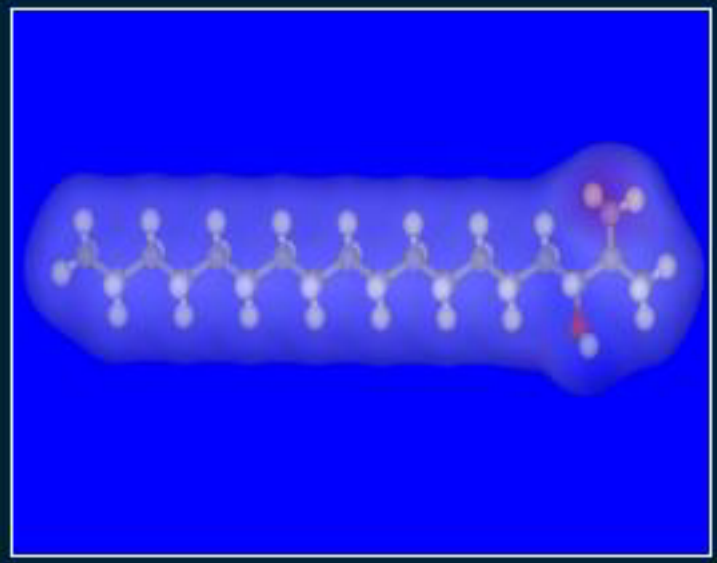


ES-285

Clinical Development Plan

ES-285 – Structure & Mode of Action

Mactromeris polynyma



ES-285 inhibits the Rho factor controlling actin microfilaments leading to:

- Changes in morphology and cell adhesion
- Triggering of apoptosis in tumor cells

ES-285 Initial Phase I Trials

SCHEDULE	TUMOUR TYPE	COUNTRIES	1st PATIENT	STATUS
3 hrs/d x 5 3 weeks	Solid tumours	EU	Aug 2003	Ongoing
24 hrs / 3 weeks	Solid tumours	EU	Nov 2003	Ongoing
3 hrs / 3 weeks	Solid tumours	EU	Jan 04	Ongoing
3 h/d weekly	Solid tumours	EU	July 2003	Ongoing

ES-285 – Clinical Dev. Plan

Summary

Broad and strong clinical development pipeline

- Four innovative compounds in clinical development
- Different modes of action
- Total of 33 studies ongoing in 15 cancer indications

Financials

Maria Luisa de Francia
Group Finance Director

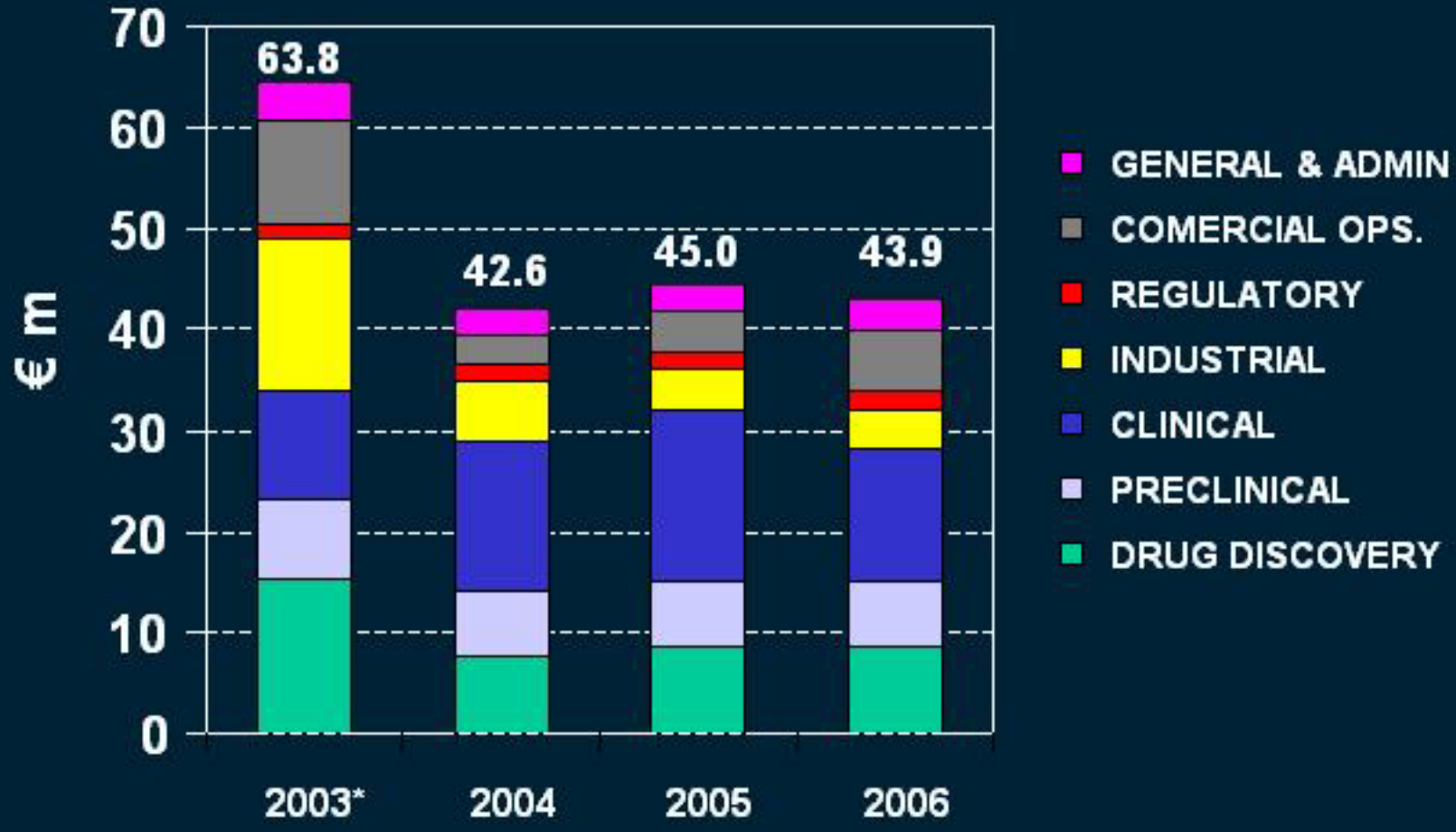
Reduction in Total Expenses

Amounts expressed in € m

	PRE-CLOSING					
	2003	2004	04 *vs* 03	%	2005	2006
R&D	22.7	14.3	-8.4	-37%	14.8	15.4
CLINICAL	10.7	14.8	4.1	38%	17.3	13.3
INDUSTRIAL	14.9	6.4	-8.5	-57%	4.2	4.4
REGULATORY	1.5	1.6	0.1	7%	1.7	1.7
COMMERCIAL OPS.	10.3	2.7	-7.6	-74%	4.0	6.0
GENERAL & ADMIN.	3.7	2.8	-0.9	-24%	3.0	3.1
TOTAL EXPENSES	63.8	42.6	-21.2	-33%	45.0	43.9

Reduction in Expenses by Department

2003 expenses reduced by 33 % in 2004 budget



(*) 2003 pre-closing

Increase in Clinical Department Budget

€ m	Pre-closing 2003	Budget 2004	03 vs 04	%
Clinical trials	7.9	12.2	+ 4.3	+ 55
Overhead and General	2.3	1.8	- 0.5	- 22
Scientific development	0.5	0.8	+ 0.3	+ 60
Total	10.7	14.8	+ 4.1	+ 38

Further increase of 17% over 2004 budget planned for 2005

Reduction in R&D Spend

€ m	Pre-closing 2003	Budget 2004	03 vs 04	%
Discovery	4.7	1.8	- 2.9	- 62
Medicinal Chemistry	3.9	2.0	- 1.9	- 49
Preclinical *	7.7	6.2	- 1.5	- 19
IP & IT	5.1	3.6	- 1.5	- 29
Overhead & Generals	1.3	0.7	- 0.6	- 46
Total	22.7	14.3	- 8.4	- 37

* PharmaMar USA: Impact exchange rate EUR / US$: € -0.6 m

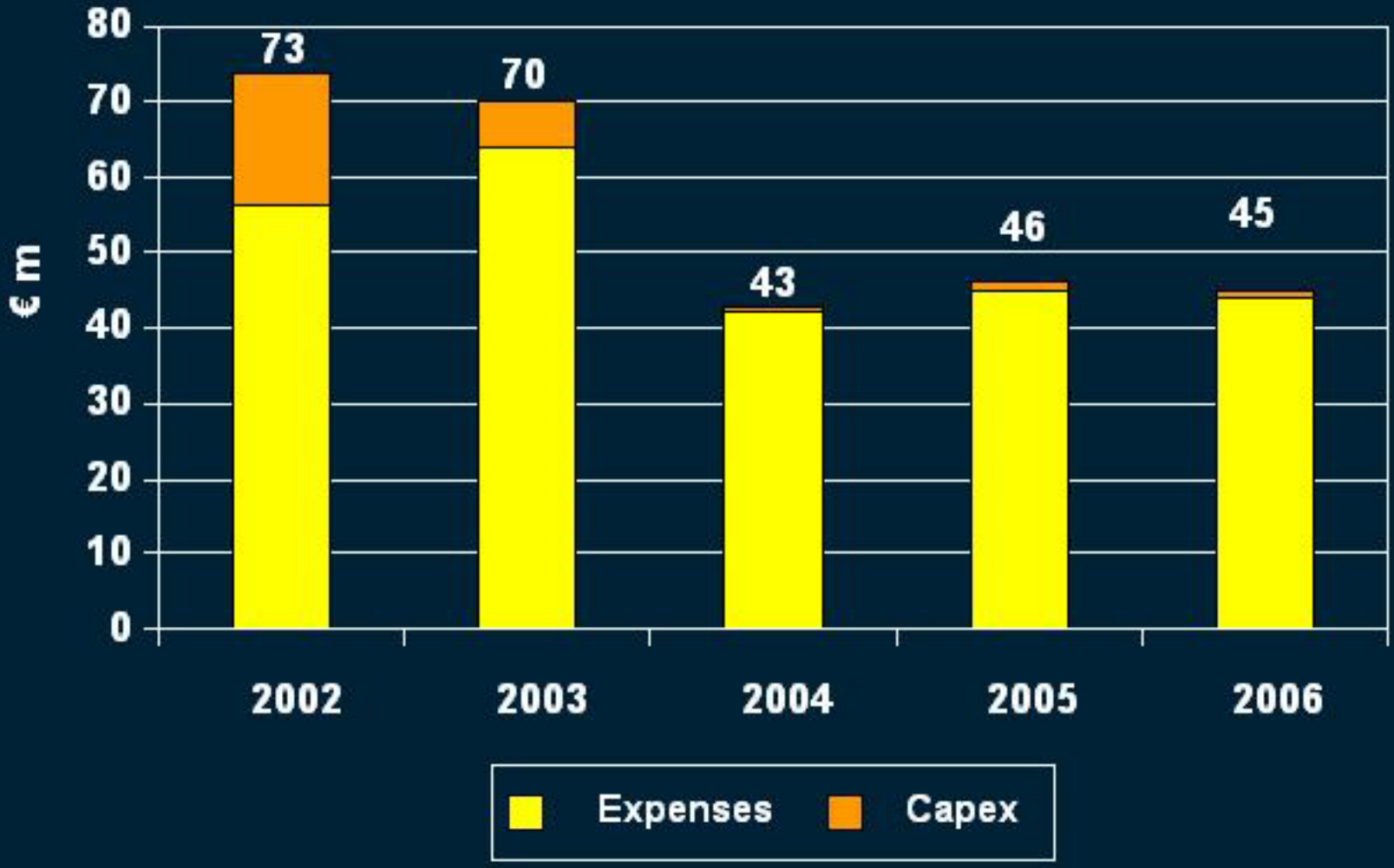
Reduction in Industrial Op. Spend

€ m	Pre-closing 2003	Budget 2004	03 vs 04	%
Marine Farming	2.2	0.1	- 2.1	- 95
Production	9.0	3.4	-5.6	- 62
Q.C. & Development	0.8	0.5	- 0.3	- 38
Quality Assurance	0.7	0.4	- 0.3	- 43
Overhead, Generals &Logistics	2.2	2.0	- 0.2	- 9
Total	14.9	6.4	- 8.5	- 57

Reduction in Commercial Op. Spend

€ m	Pre-closing 2003	Budget 2004	03 vs 04	%
Sales Force	2.7	0.0	- 2.7	- 100
Marketing & Pre-Marketing	2.5	0.1	- 2.4	- 96
Medical Affairs	0.5	0.3	- 0.2	- 40
Business Development	0.8	0.6	- 0.2	- 25
HQ Commercial Operations	3.8	1.7	- 2.1	- 55
Total	10.3	2.7	- 7.6	- 74

Cash Burn Evolution



Projected PharmaMar Income 2004 - 2006

	Expected € m	Reasoning
Yondelis™ Income	20	Conservative, includes limited sales in 2006
New Licence	25	Yondelis™ licenced for $20M in 2001 and a further $6M received in first year
Disposals	3	Sale completed
Grants	12	€ 7 m received in 2003
Total	60	

Zeltia – Consolidated Cash Position Jan 04

	€ m
Net cash position 30-09-2003	101
Treasury stock at market value*	10
Disposal real estate**	6
Net cash burn third quarter	(17)
Net cash position today	100

* Treasury stock valued at theoretical value (€1.4/share) in the financial statements
** € 6 m received by Zeltia in January 2004

Zeltia - Projected Cash Flow

€ m	2004	2005	2006
Group Initial Balance	100	63.2	23.2
Operating cash flow PharmaMar	- 34.5	- 33.5	- 3.4
Op. cash flow parent company & net financial	- 6.2	- 9.2	- 9.6
Group long term loans cancellation	- 3.4	- 4.4	- 4.7
Free cash flow Chemical Division	10	10	10
Group capex	- 1.5	- 1.7	- 1.9
Genomica investments R&D	- 1.2	- 1.2	- 1.2
ACUMULATED CASH FLOW	63.2	23.2	12.4

Conclusions

- Cash resources of the group extended to 3 years, sufficient to launch first Yondelis™ indication
- Gives additional year´s cash over previous projections
- PharmaMar's cash burn reduced from € 70 m to € 43 m (39%) in 2004
- Of the € 70 m, expenses represented € 63 m, amounting to a reduction of 33% in PharmaMar running costs
- Cash burn in 2005 and 2006 remains stable at around € 45 m

Enables delivery of business plan without further capital increase

Closing Remarks

Isabel Lozano
PharmaMar CEO

Consequences of the EMEA Decission

Short term

- Delay in our expectations regarding sales of Yondelis™ in 2004
- Minimal impact on cashflow: limited sales potential in STS relative to cash needs for commercialization

Long term

- No effect on expected launch dates for other indications of Yondelis™
- Development of rest of clinical pipeline unaffected
- Limited impact on preclinical pipeline

Rapid Implementation

- Rightsizing to achieve objectives
- Focus on efficient development of advanced pipeline
- Overall budget reduced by 33% while increasing resources available for clinical development
- Key capabilities maintained across the board

Rapid Implementation

- Rightsizing to achieve objectives
- Focus on efficient development of advanced pipeline
- Overall budget reduced by 33% while increasing resources available for clinical development
- Key capabilities maintained across the board

Focus on Clinical Throughput

- Extensive development of four compounds in clinical pipeline with three indications for potential registration in 2006
- Prioritized preclinical pipeline: PM-10450 to begin clinical trials within one year
- Several new compound families under active preclinical development secure pipeline renewal
- Open to partnering maximises speed and prospects of drug development

Delivering the Strategy Within Our Means

- Starting cash position of € 100 m
- Conservative estimate of € 60 m in medium term revenues
- Backing of the Zeltia group
- Broad clinical development plan delivering clinical results in many cancer indications and treatment options
- J&J: a first-class partner
- Determined to deliver the strategy

Platform to achieve first registration of Yondelis™ in Europe by 2006

Abbreviations and Acronyms Used (I)

- ALL: Acute Lymphocytic Leukemia
- ALT: Alanine Transaminase (hepatic enzyme)
- AML: Acute Myeloid Leukemia
- APL: Aplidin®
- AST: Aspartate Transaminase (hepatic enzyme)
- ATU: Autorisation Temporaire d'Utilisation (Temporary Authorization of Use)
- BM: Bone Marrow
- CPK: Creatine Phospho Kinase (muscular enzyme)
- COMP-EMEA: Comittee for Orphan Medicinal Products – European Agency for the Evaluation of Medicinal Products
- COMPARE (NCI): National Cancer Institute Program for anticancer drug testing in cell lines.
- CPMP: Comittee of Proprietary Medicinal Products
- DD: Drug Discovery
- DLT: Dose Limiting Toxicity
- EGF: Epidermal Growth Factor
- EORTC: European Organization for the Research and Treatment of Cancer
- FPI: First Patient In
- GI: Gastro Intestinal
- HN: Head and Neck cancer
- IC_{50}: Inhibitory Concentration of 50% of cells
- ICON-4: International Collaborative Ovarian Neoplasm 4 (clinical trial)
- IRB: Institutional Review Board
- JDP: Joint Development Plan (between PharmaMar and J&J)

Abbreviations and Acronyms Used (II)

- JNK: Enzyme involved in the apoptosis regulation
- MDR: Multi Drug Resistance
- MM: Multiple Myeloma
- MR: Minor Response
- MSKCC / MSC: Memorial Sloan Kettering Cancer Center
- MTC: Medullary Thyroid Carcinoma
- MTD: Maximum Tolerated Dose
- NCI: National Cancer Institute
- NHL: Non-Hodgkin Lymphoma
- NSCLC: Non Small Cell Lung Cancer
- OSR: Overall Survival Rate
- PB: Peripheral Blood
- PD: Progressive Disease
- PFS: Progression Free Survival
- PTS: Patients
- RD: Recommended Dose
- RR: Response Rate
- SCLC: Small Cell Lung Cancer
- SD: Stable Disease
- STS: Soft Tissue Sarcoma
- TBD: To Be Determined
- TTP: Time To Progression
- VEGF: Vascular Endothelial Growth Factor

Definitions and Terms

- Analysis: status of clinical study when it is terminated and data are being analyzed.
- Arm: group of patients included in a clinical study with similar characteristics and treatment
- Completed: status of clinical study when data analysis is finalized
- Randomized: design of a clinical study which implies inclusion of patients at random in different treatment arms.
- Recruitment: period of inclusion of patients in a clinical study

Expected Newsflow and Major Congresses

with Active PharmaMar Participation

2004

February 26	FY03 Zeltia S.A. Results
March 27-31	AACR Congress, Orlando Preclinical congress. Three abstracts already accepted
April 29	1Q '04 Zeltia S.A. Results
June 5-8th	ASCO Congress, New Orleans Expect to present data on Yondelis™ as a single agent and in combinations Also expect to present data on Aplidin® in solid tumours
May/June	Annual Shareholders Meeting
July 22	2Q '04 Zeltia S.A. Results
28 Sep-Oct 1	EORTC-NCI-AACR Congress, Geneva Preclinical congress. Expect to present further data
29 Oct –2 Nov	ESMO Congress, Vienna Expect to present further results of Yondelis™ in combination Also expect to present further data on Aplidin® in solid tumours
October 28	3Q '04 Zeltia S.A. Results