From Tactical to Strategic Outsourcing in Mid-Size company

Thursday 8th October, 2015

PCMG Outsourcing Workshop

Almirall

Solutions thinking of you

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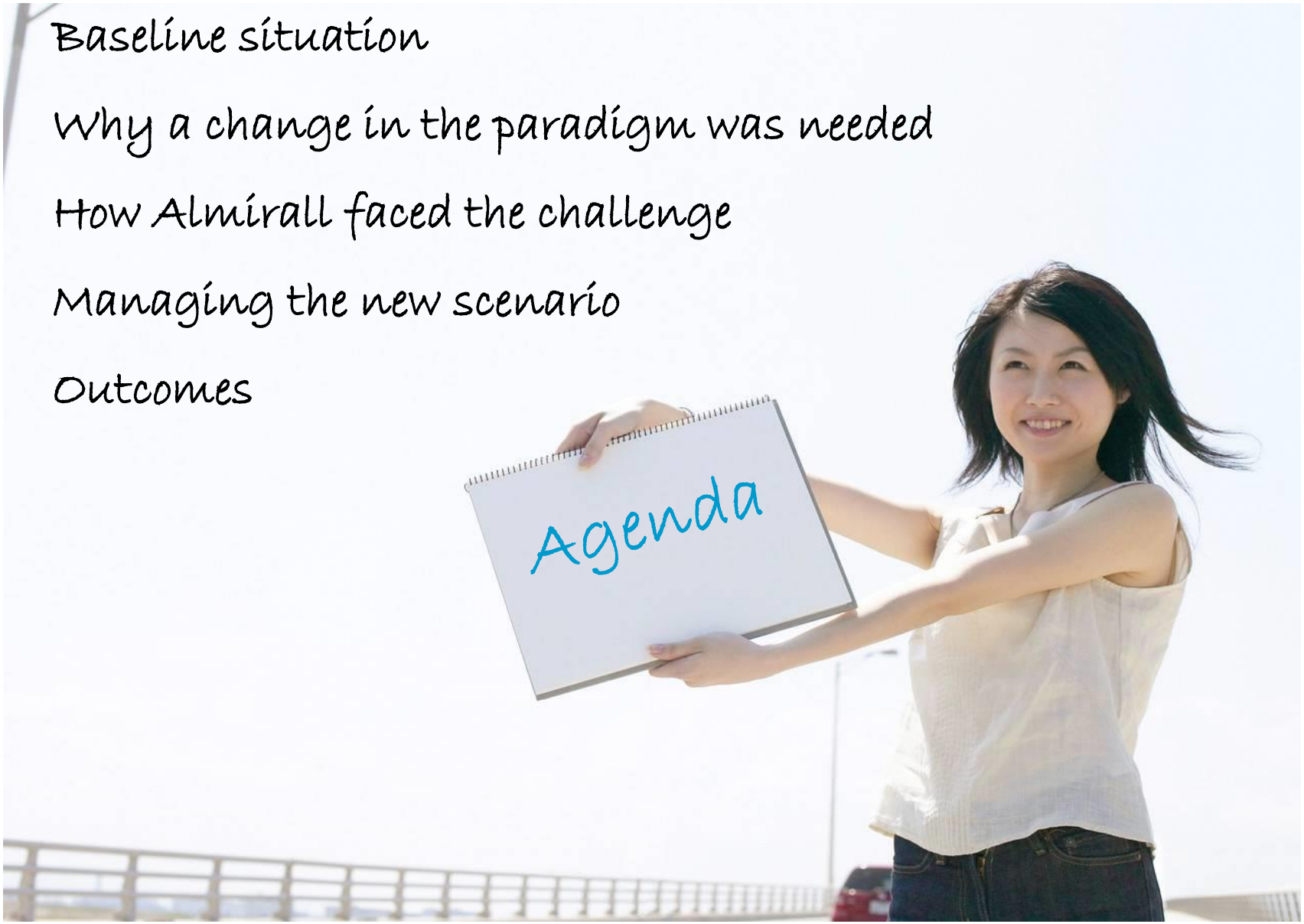
- Baseline situation
- Why a change in the paradigm was needed
- How Almirall faced the challenge
- Managing the new scenario
- Outcomes



Objective

- Share Almirall experience with you!

Almirall at a glance

A global company that covers the whole of the drug value chain

Almirall in figures in 2014

14 affiliates in Europe and North America and trading capacities in **22** countries

Almirall products in over **70** countries on **5** continents

2130
employees

843
employees in affiliates

+250
employees in R&D

€ 1,407 MM
Total revenues

€ 786 MM
Net sales

12.8%
R&D investment vs sales

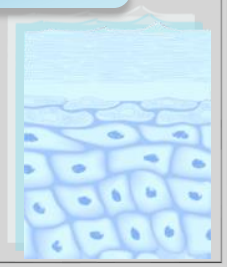
R&D capabilities (Life Cycle Management)

Strategic Therapeutic Areas

One of Almirall's priorities is to promote proprietary R&D focused on our strategic therapeutic areas

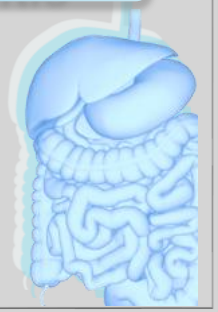
Dermatology

- *Acne*
- *Rosacea*
- *Atopic Dermatitis*
- *Psoriasis*



Gastrointestinal

- *IBS-c*
- *Ulcerative Colitis*



Pain

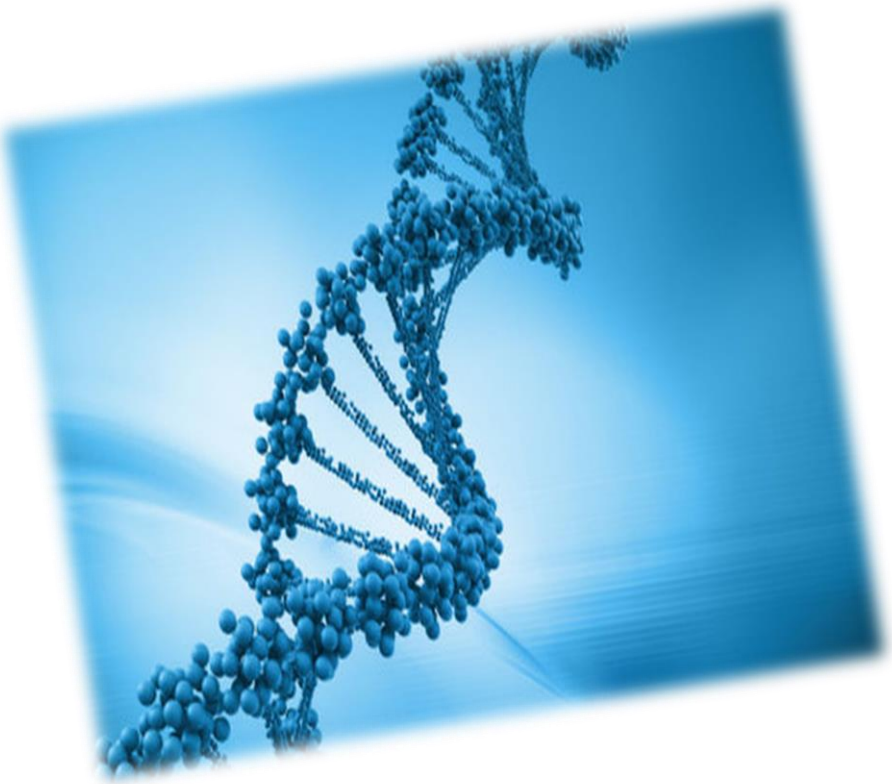
- *Cancer pain*

NCEs / Repositioning / Reformulation

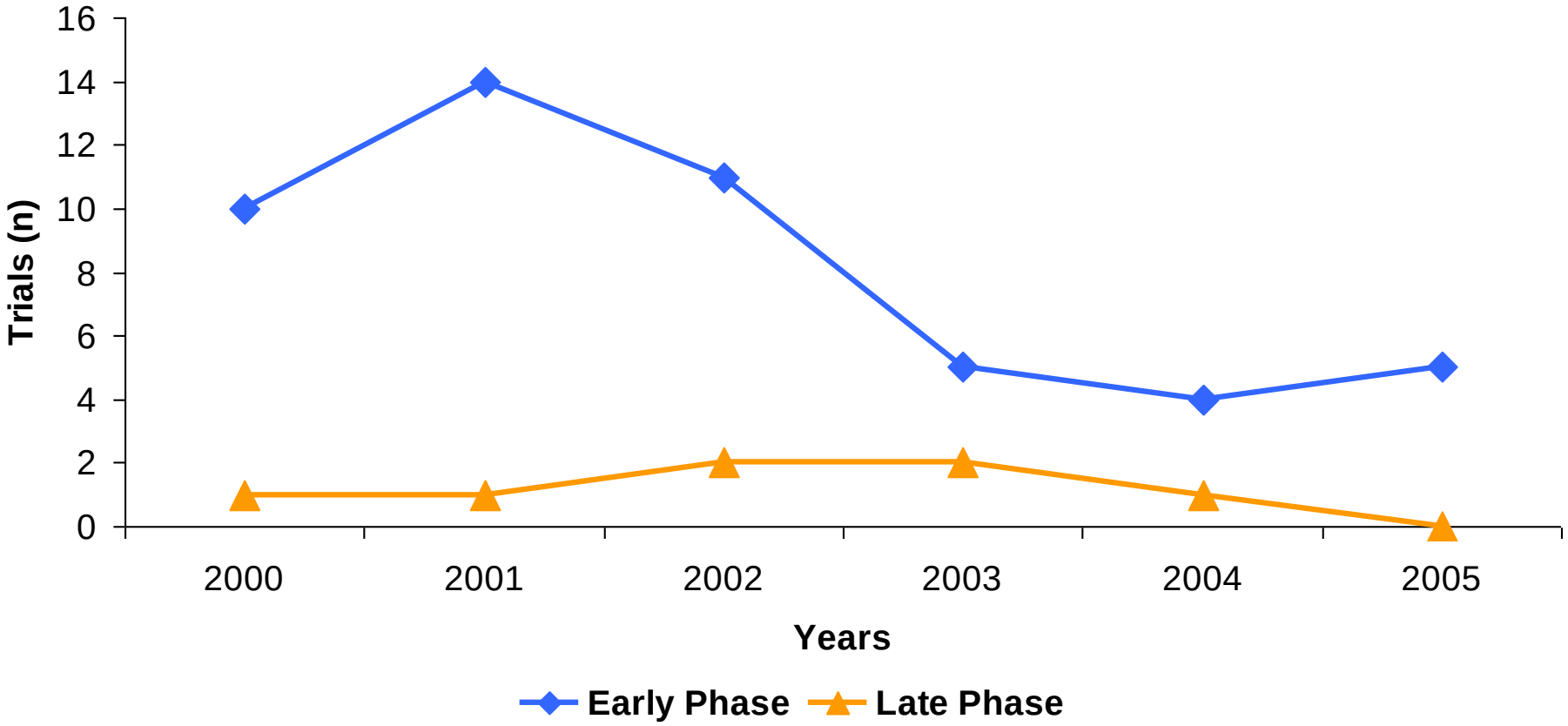
- *Oral*
- *Topical for skin*

Almirall Outsourcing Model before 2005

Every study and company is unique



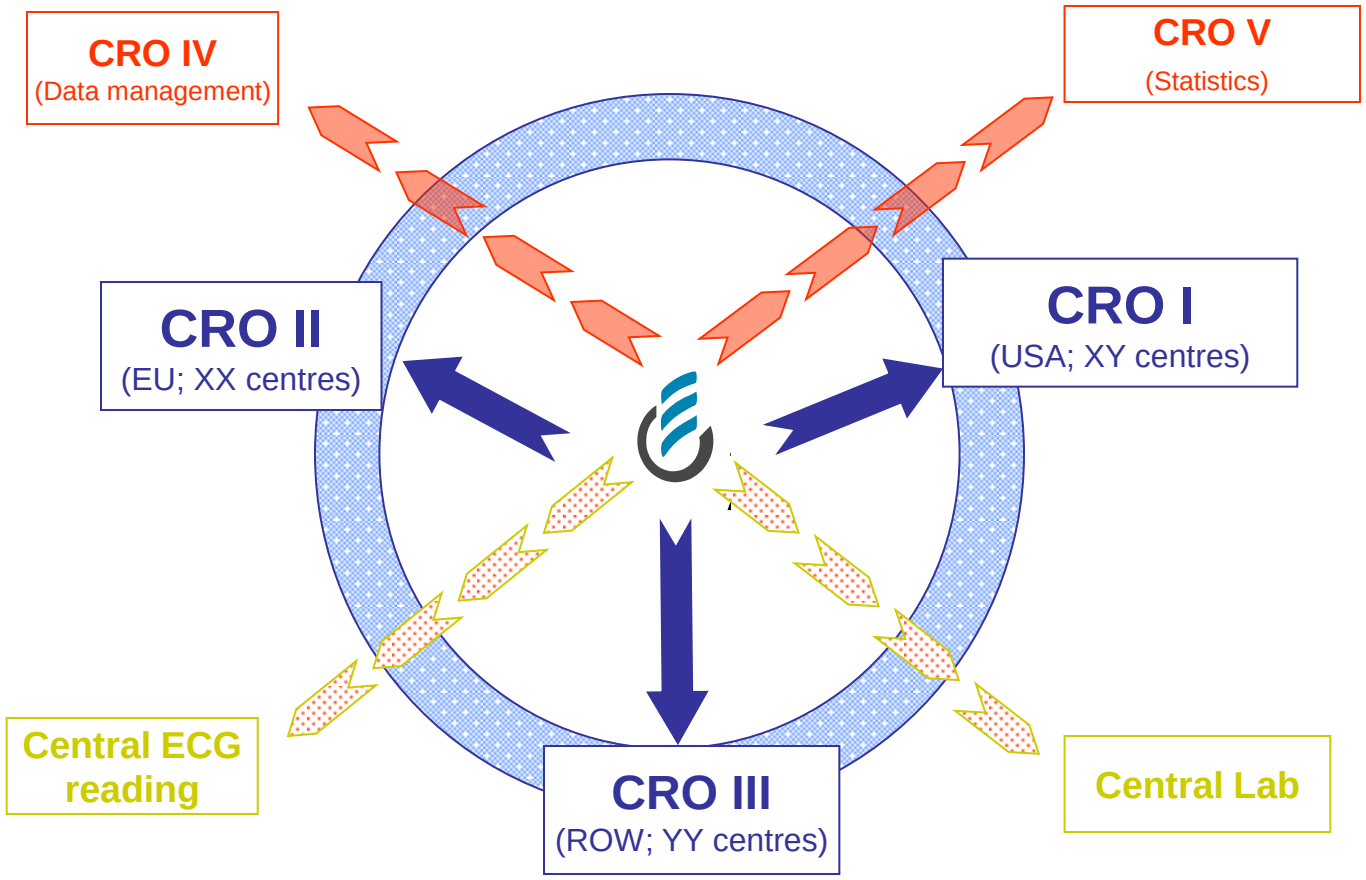
Early vs Late Phase Trials evolution: 2000-05



Almirall outsourcing approach 2000-05

- **Phase I and IIa trials: preferred providers**
  - Master agreements with Phase I Units, specialised Sites, specialised local CROs, etc.
  - Preferred providers for Data Management and Statistics
- **Phase IIb and Phase III**
  - Several providers for experimental phase (CROs)
  - Direct vendors contract: ECGs, Labs, IVRS, etc.
  - Preferred providers for Data Management and Statistics

Case Study for a Phase IIb/III trial



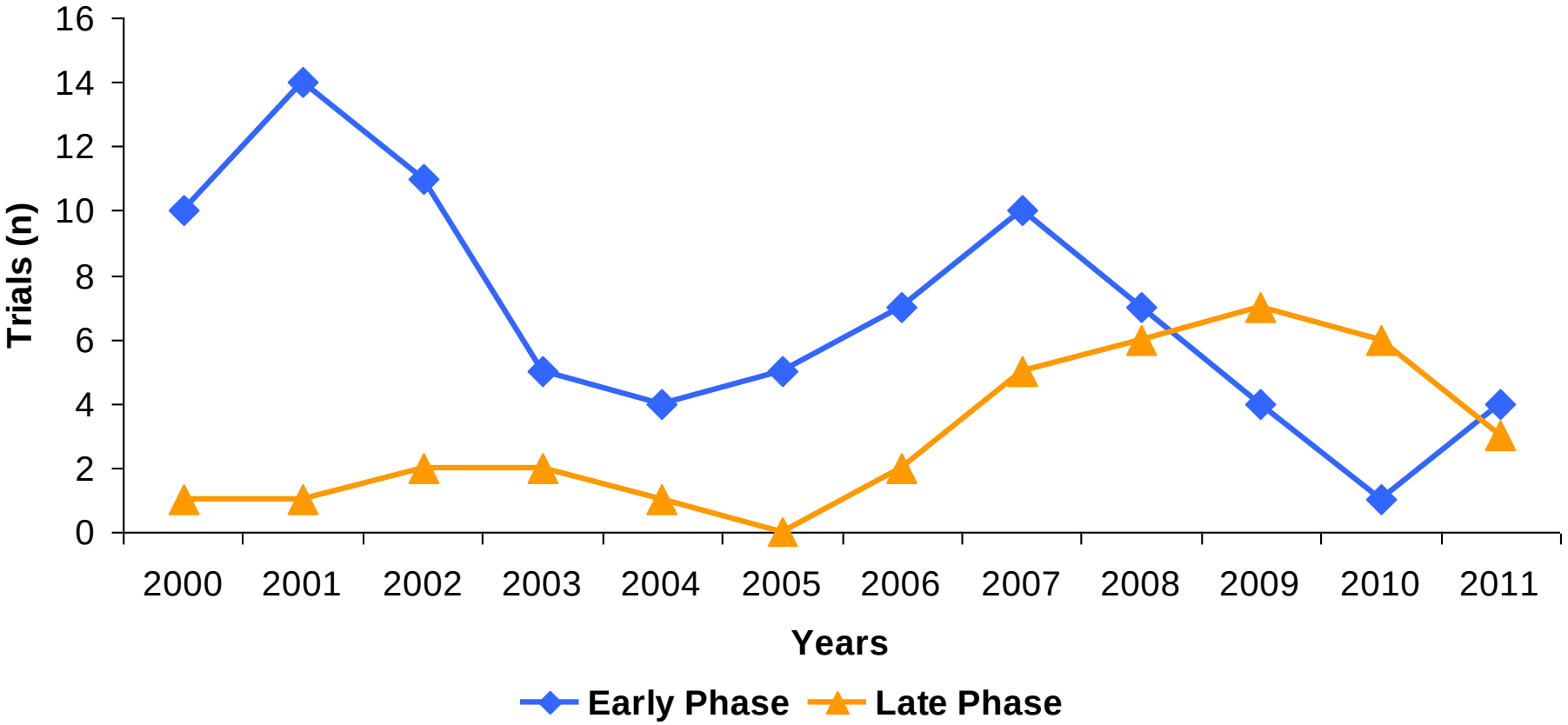
Results of this model

- Seven Services agreements to be negotiated
- Project Management located within Almirall
- High number of FTEs at Almirall devoted to this model
- Lack of synergies from the financial and operational point of view
- Huge difficulties to align ALL vendors
- High level of communication
- Dilution of responsibilities (sponsor side)

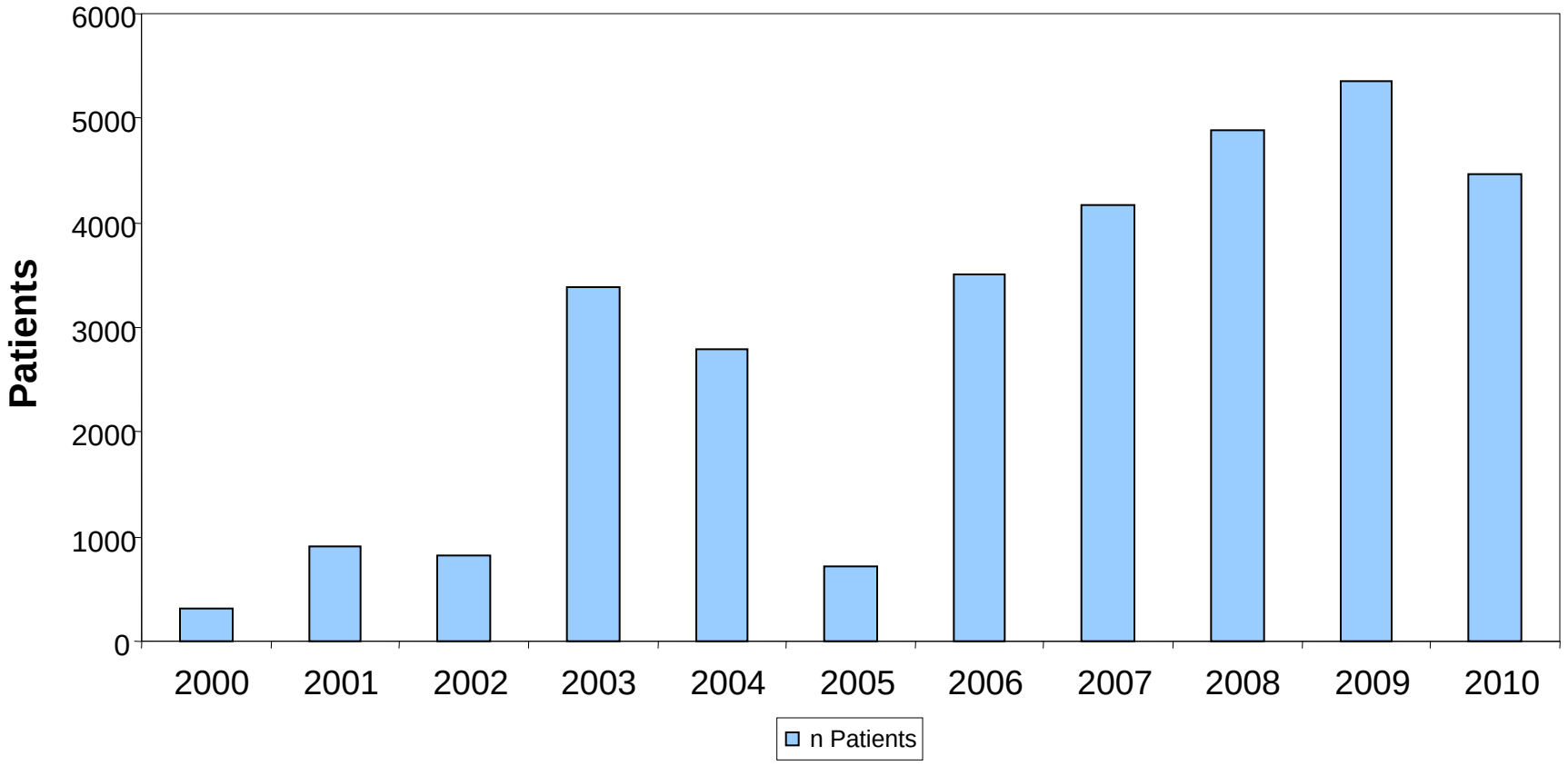
Positive cost/benefit balance only for small trials (up to Phase IIa), Phase III whole program need different approach.

Why a change in the paradigm was needed?

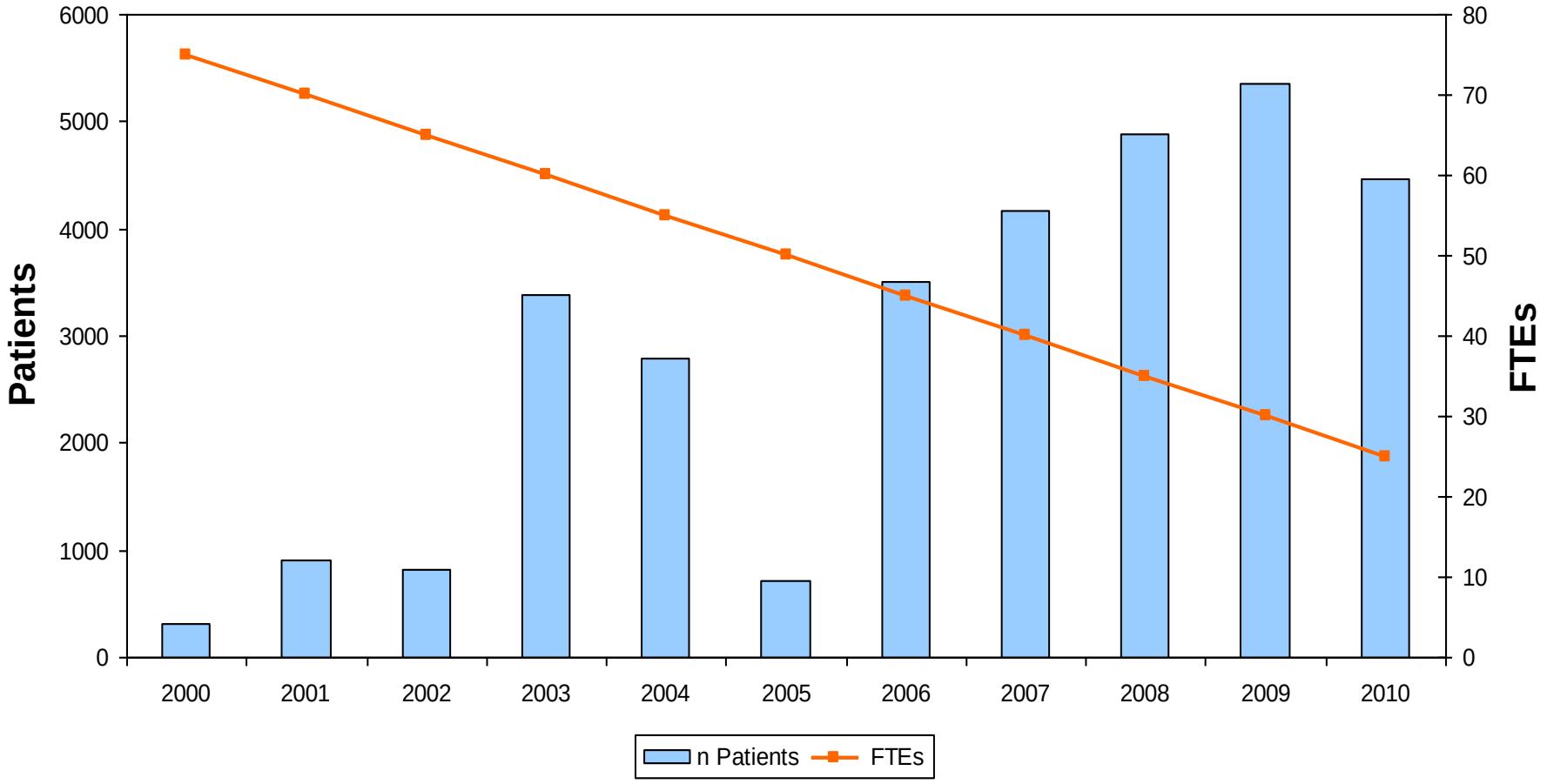
Early vs Late Phase Trials evolution (2000-2011)



Active Patients per year



Facts & Figures



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Did we have an option?

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How we faced the challenges?

Previous work to be done at home

- Number of trials to be outsourced
- Core activities to do in house
- Clear communications of activities per trial/project
- Clear definition of the deliverables
- Timelines per trial/project
- SOPs to be used
- System to manage the program
- Reporting, Meetings & Training required

How we selected the partner

- Extensive assumptions document (activity, deliverables, quality definition, expectations,
- Clear Protocols and Outlines
- Grid for budgeting (Including Unit Cost)
- Financial approach proposal by CRO
  - Payment schedule
  - Synergies
- Internal Negotiation Team
  - Operational, Scientific, Finance, Purchasing, Legal, etc. etc.
  - Clear rules & roles
  - Clear established criteria for CRO selection: 3C (Capability, Compatibility and Cost)

Managing the new scenario

How to ensure the deliverables

- Kick-off, F2F and T/C
- Define the Project /Study Information Plan
- Establish clear metrics to be achieved:
  - Speed and Quality Metrics
- Systems to manage the trials and CRO performance:
  - Global Clinical Portal (Clinical Data & Documents)
  - Impact as CTMS (Operational data)
- Establish the Governance structure

Almirall-CRO: Governance Structure

- **Executive Committee (EC)**

  - Senior executives
  - No more than five per company
  - At least twice a year (with additional meetings as required by any of the parties)

- **Objectives**

  - Review the project from the operational and financial point of view
  - Review key metrics for performance evaluation
  - Resolve issues

The outcome

Positive Outcome

- **Added value by partner**
  - Technology integration
  - Geographical coverage & expertise
  - Therapeutic expertise
- **Learning curve effect**
  - Quicker start up phase for the clinical trials
  - Higher commitment by the Investigators, Top Management of CRO
  - More efficiency in reviewing plans, docs,
- **Allows for mind set change on both sides**
  - Operational and Financial flexibility

Lessons Learned

- **Precise scoping is key to avoid conflicts**
  - Move from task oriented to deliverable based outcome
  - Clear definitions of deliverables and responsibilities
- **Take some time to merge corporate cultures**
- **Gap analysis on team member skills**
  - Technical skills vs Managerial skill
- **Watch micro-management**
  - Old habits sneak back in

The outcome so far …

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Many Thanks!!

Questions?

Back ups

Speed/Performance Metrics (I)

Metric Concept	Time frame (planned)	Time frame (actual)
1. Qualification sites: 90- 95% done by		
2. Health Authorities Submission: 90-95% done by		
3. Ethics Submissions: 90-95% done by		
4. Sites initiated: 90-95% done within 40-60 days from First SIV to Last SIV. ▪ This metric will have to be detailed by country. It will also have to be related to First Investigator Package Plan approved (IPP)		
5. Patients randomised: 30%, 60% and 100% by		
6. Clean patients: 30%, 60% and 100% by ……. ▪ Clean patients included vendors and safety reconciliation		
7. Soft Lock		
8. Data Base Lock		
9. Top Line Results		

Quality Metrics (I)

Metric Concept	Range/Number (planned)	Range/Number (actual)
1. % Amendments to the protocol (Relevant and Administrative)		
2. % Unacceptable Forced FTEs after BTR (< 10%)		
3. Frequency of Routine Monitoring Visits (%): ▪ < 2 weeks; >2 and < 4 weeks; >4 weeks		
4. Queries ratio/page/patient/vendor		
5. Turn around of queries: ▪ < 10 days; 10-30 days; >30 days		
6. Major deviations per site/country/trial		

Study Information Systems

There are two major systems that we utilize in our processes

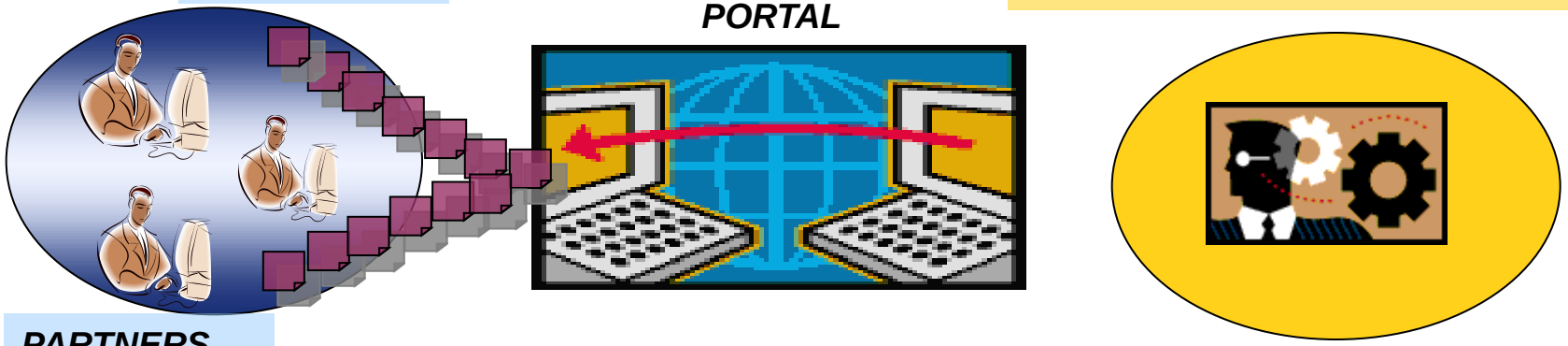
System	Description	Access
Global Clinical Portal **(GC Portal)**	▪ Almirall Document Management System used to exchange study documents, database transfers & reporting between Almirall, CROs and partners. ▪ Allows any format document sharing, reviewing & updating.	Read / Write
IMPACT	▪ International Management Package of Administration of Clinical Trials. ▪ Management, tracking and reporting tool for study/countries/sites status, event dates, issues & recruitment figures	Select users Read / Write

Clinical Trial Information Systems

PROVIDERS

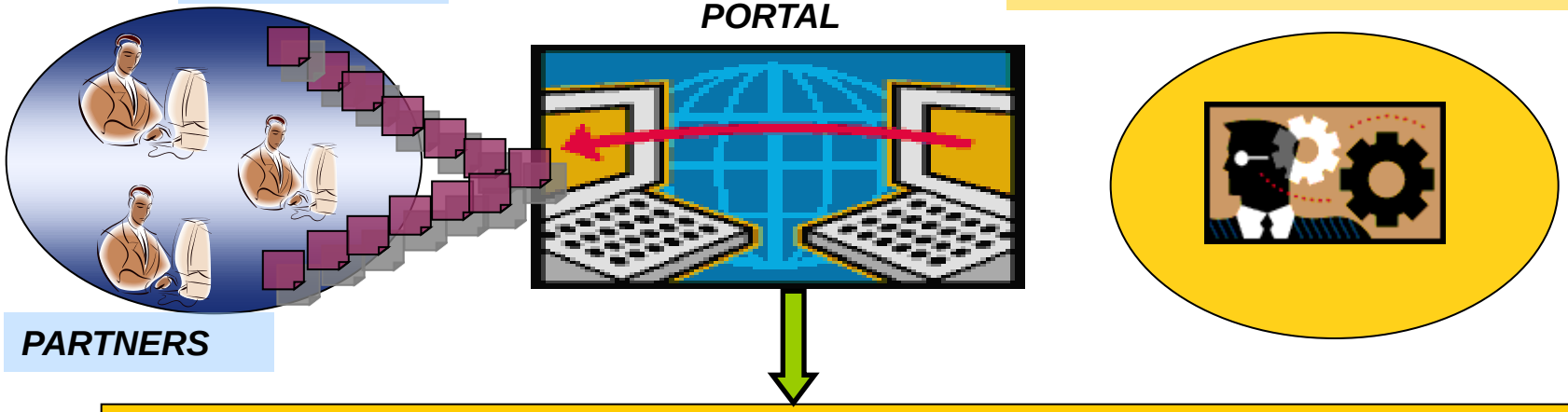
PORTAL

ALMIRALL PROJECT MANAGEMENT



PARTNERS

Clinical Trial Information Systems



REPORTING TOOL (Business Objects)

CLINTRIAL

DOCUMENTUM

IMPACT

*PORTAL

ARIS

SAS

Essential Documents

Trial Progression

MS Project

Status files

Pharmacovigilance

*Almirall owner

Almirall

Global Clinical Performance Metrics

MEDIAN DURATION (DAYS)	PHASE I			PHASE II			PHASE III		
	Target*	Almirall		Target*	Almirall		Target*	Almirall	
Total Study Duration	703	905	▼	639	664	▶	766	503	▲
Study Start Up	117	91	▲	133	118	▶	125	151	▼
Patient Enrolment	242	32	▲	332	52	▲	339	167	▲
Data Clean-Up	93	32	▲	50	37	▲	59	40	▲
Top Line Results Analyses	N/A	14	--	N/A	7	--	N/A	6	--

***Reference: CMR INTERNATIONAL PERFORMANCE METRICS PROGRAMME / SOURCE**

Trial Performance Legend

Performance Improving	> 5%	▲
Performance Staying about the same	5% - 15%	▶
Performance Declining	> 15%	▼

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Almirall outsourcing from 2005 onwards

- **Phase I and IIa trials of early projects:**
  - Master agreements with Phase I Units, specialised Sites, specialised local CRO, etc.
  - Preferred providers for Data Management and Statistics
- **Full Phase III Programme with the same NCE:**
  - Full services CROs, including contract with vendors (ECG, Lab, IVRS, EDC, etc.)
  - Overall Project Management in house

Managing a Phase III Program

- What needed to be outsourced
  - Trials
  - Activities
  - In a given time
- CRO selection process
  - RFQ and bid defense
  - Negotiation Team established at Almirall
- CRO selection criteria
- CRO and Program management
  - Tools to manage the trials
  - To follow up performance of the CRO
  - Kick-off, F2F, T/C, etc.
  - Executive Committee

Almirall Program to be subcontracted

TRIALS	PHASES	N	COUNTRIES
2	Phase III clinical trials to demonstrate efficacy and safety during one year	> 1500 COPD randomised patients	24 countries WW
5	Phase I trials in healthy volunteers, COPD patients and special populations	Healthy Volunteers, Renal insufficiency and COPD patients	Few countries
3	Phase IIa trials to better profile the product	COPD patients	Few countries

How was the project outsource

- Only “core activities” remain in house:

  Protocol writing, SAS Programming, Statistical analysis (SAP)

- CRO supervision focus on:

  Clear agreement on deliverables (quality and timelines)

  Only key process to be reviewed

- CRO SOPs revision

  More than 100 from all areas in Div Med + QA+ IRRAA+ IT

- Audit Plan to CRO, Sites, and vendors

  By the CRO

  By Almirall

RFP process

- Assumptions document

  Distribution of activities

  Clear explanation of the activities

- Protocols and outlines
- Grid for budgeting

  Including Unit Cost

- Financial approach proposal by CRO
  - Payment schedule
  - Synergies
- Negotiation Team
  - Operational, Scientific, Finance, Purchasing, Legal, etc. etc.

Activities Distribution List

Group of activities

ACTIVITY	ALMIRALL	CRO	DESCRIPTION
STUDY MANUAL		X	
STUDY SET UP		X	
STUDY CONDUCT		X	
STUDY CLOSE		X	
DATA MANAGEMENT		X	
STATISTICS	X		
REPORT		X	

Main criteria to select a CRO for Phase III

Capability:

- Previous experience in the therapeutic area
- Worldwide presence
- Feasibility studies
- Investigator's identification
- Experience in local requirements
- Team expertise assigned to the trial
- Phase I Units, ECGs, Lab, IVRS, etc.

Compatibility:

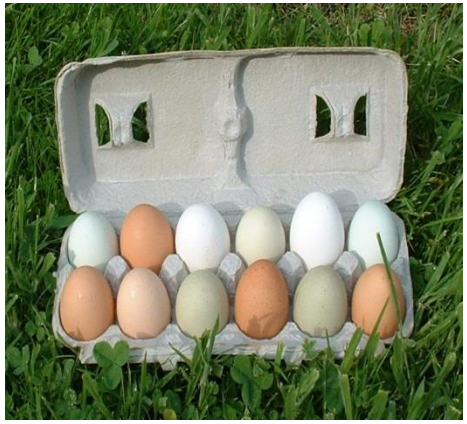
- Size of companies
- Legal requirement
- Bid defense meeting
- SOPs and process

Cost

- Budget grid (the same grid to every one to compare properly)
- Unit cost
- Savings due to sinergies
- Payment schedule

Conclusion: Almirall outsourcing strategy

- Base on the type of company we are
- Resources we have
- Complexity of the projects we deal with



VS

Phase I to IIa

Phase IIb to Phase III