



# Annual General Meeting of PAION AG

Aachen, 20 June 2007

## Disclaimer

It is important to note that this information contains forward-looking statements which are based on the currently held beliefs and assumptions of the management of PAION AG, which are expressed in good faith and, in its opinion, reasonable. Forward-looking statements involve known and unknown risks, uncertainties and other factors, which may cause the actual results, financial condition, performance, or achievements of PAION AG, or industry results, to differ materially from the results, financial condition, performance or achievements expressed or implied by such forward-looking statements. Given these risks, uncertainties and other factors, recipients of this information are cautioned not to place undue reliance on these forward-looking statements. PAION AG disclaims any obligation to update these forward-looking statements to reflect future events or developments.

NOTE: Generally figures are given in EUR. USD amounts were converted by using an exchange rate of 1.35 USD per EUR with the exception of the down-payment made by Forest which was received in USD and where the historical exchange rate was applied.

# Development in the projects

**Dr. Mariola Söhngen**  
**Chief Medical Officer**

Annual General Meeting  
Aachen, 20 June 2007



## PAION wants to make stroke a manageable disease

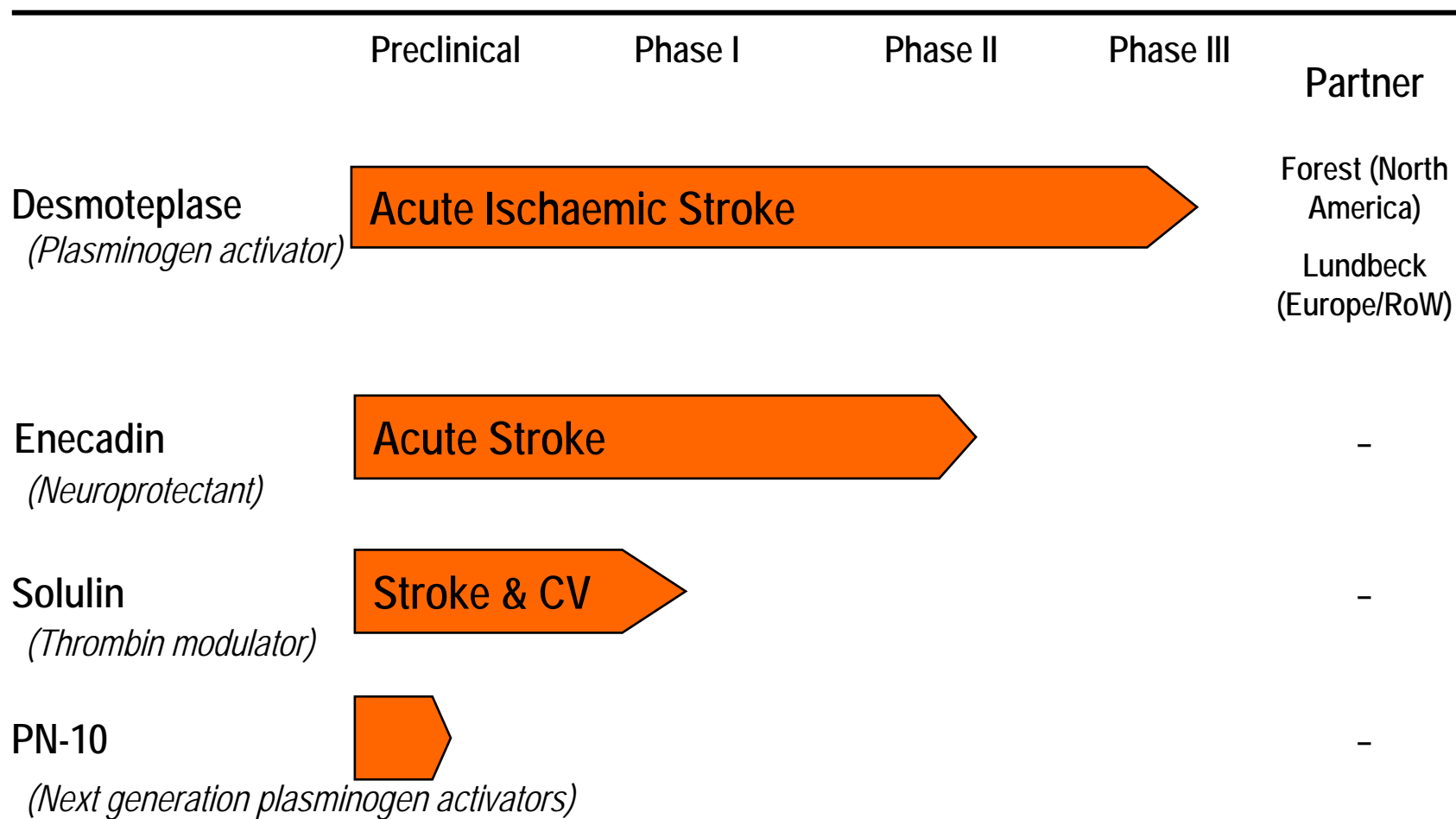
### Mission

- Become a leader in developing and commercializing drugs for treating stroke and other thrombotic diseases

### Strategy

- Focus on clinical development
- In-licensing approach to build integrated drug portfolio
- De-risking through cooperation with experienced partners
- Adding value by maintaining (co-)promotion rights

## Development pipeline



## Solulin overview 1

- Market positioning
  - Anti-inflammatory thrombin modulator: “intelligent” anticoagulant with high potential for indications where other anticoagulants are contra-indicated or unsafe
  - Potential in stroke, reduction of neuronal damage and thrombotic diseases
- Product Characteristics
  - Recombinant human thrombomodulin
  - 3rd-party product analogue has shown clinical efficacy in prevention of DVT post-hip surgery and treatment of DIC (sepsis)
- Activities 2006/2007
  - Intensive exchange with authorities after the Tegenero catastrophe
    - Task packages for analytic and preclinical studies
  - Preparations for the start of a Phase I study (within a *scientific-advice-procedure* with the BfArM)
  - Establishment of submission options in other countries

## Solulin overview 2

- Activities 2006/2007
  - Intensive exchange with authorities after the Tegenero catastrophe
    - Task packages for analytic and preclinical studies
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## Enecadin overview

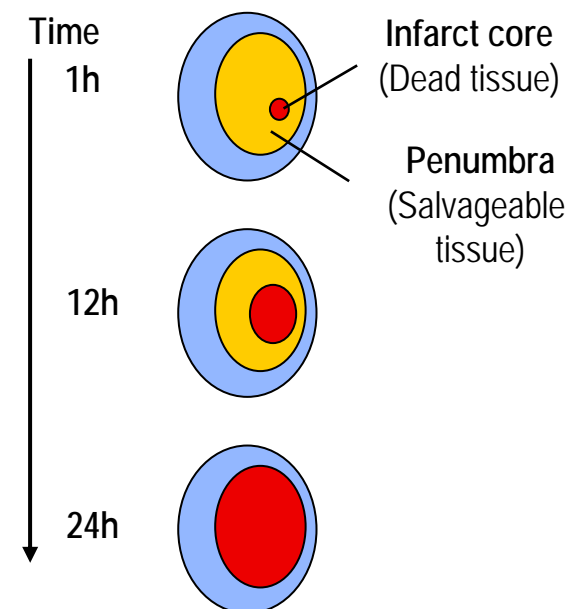
- **Market positioning**
  - Neuroprotective agent for the treatment of acute ischaemic stroke
  - Significant potential as stand-alone treatment and combination therapy with Desmoteplase or other therapeutic approaches
- **Product characteristics**
  - Sodium and calcium channel blocker
  - Good safety profile expected (based on Phase I results)
- **Pre-clinical data**
  - Significant reduction of infarct size up to 12 h after stroke in rats
  - Ameliorates behavioural deficits 7 days after permanent MCAO in rats

## Enecadin overview 2

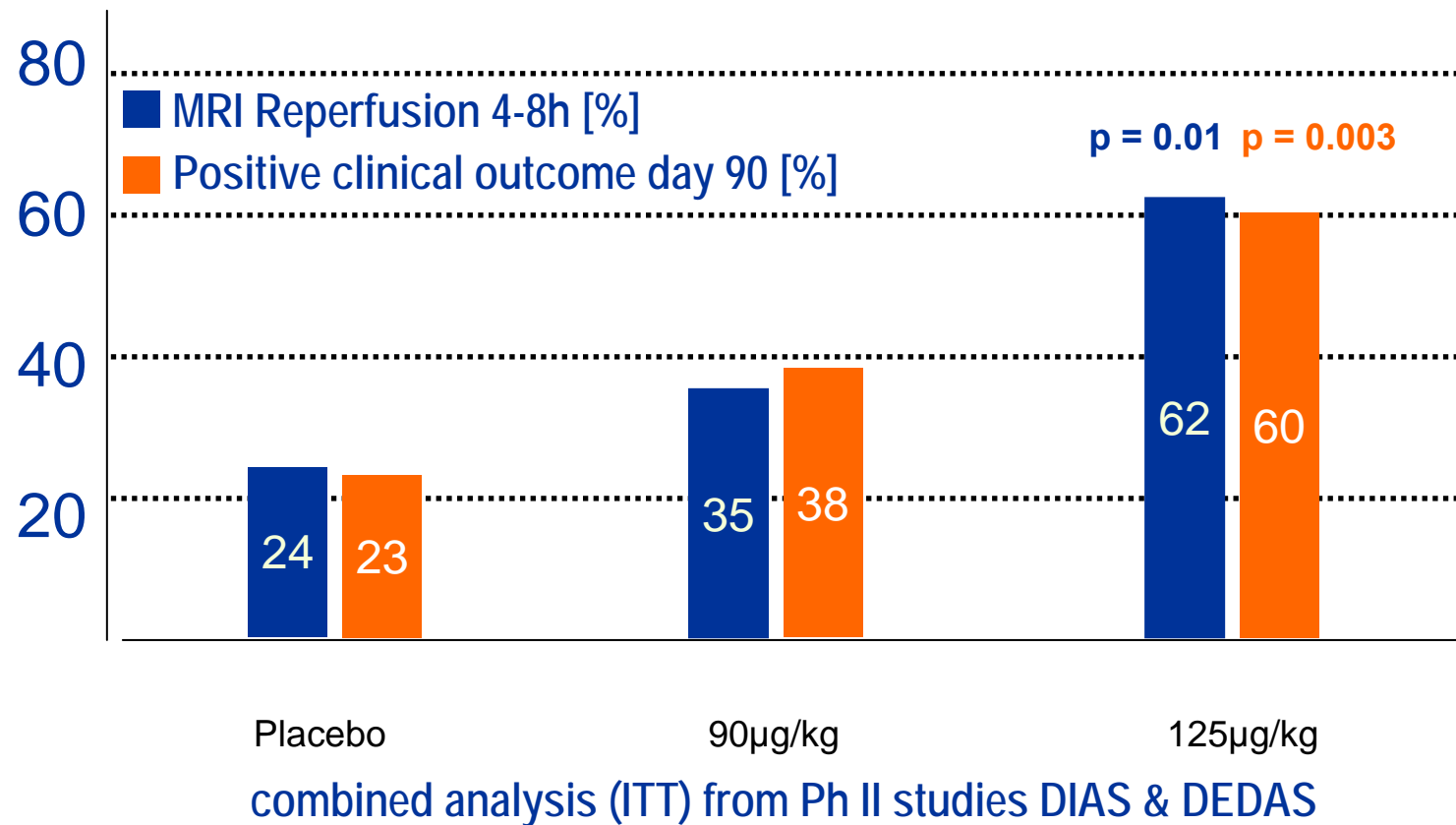
- **Aktivities 2006/2007**
  - Start Phase IIa study (TEST)
  - Extensive discussions with authorities
  
  - Recruitment in the first dose tier (TEST) completed in June 2007
  - Safety data package

## What is an ischemic stroke?

- Two types of stroke:
  - Ischemic: about 88%, caused by a clogged vessel in the brain
  - Haemorrhagic: about 12%, caused by the rupturing of weakened blood vessels in the brain
- Series of events:
  - Clogged vessel in the brain interrupts supply with blood and oxygen: ischemic stroke
  - Deprived of oxygen, nerve cells in the affected area die: infarct core
  - Nerve cells in the surrounding, hypo-perfused area are still alive but at risk of gradually dying: penumbra
  - Series of subsequent endogeneous events causes further damage of the brain: ischemic cascade
- As a result:
  - Basic life functions are destroyed or seriously damaged
  - About 40% die within one year
  - Majority of survivors need permanent external resources to manage their lives



## Desmoteplase: Significant correlation of reperfusion and positive clinical outcome



Correlation Recan/clin: p < 0.001

## Ph III study for desmoteplase in ischaemic stroke (study acronym DIAS-2)

### Design

- Phase III dose ranging study (90 µg/kg, 125µg/kg Desmoteplase)
- Randomised, double-blind, placebo-controlled, parallel group
- Multi-centre, multinational (Europe, USA, Canada, Australia, Hong Kong, Singapore)
- 186 patients

### Primary Efficacy and Safety

- Clinical improvement at day 90 in all three stroke scales:
  - NIH Stroke Scale (improve  $\geq 8$  points from baseline or score  $\leq 1$ )
  - Modified Rankin Scale (score 0-2)
  - Barthel Index (score 75-100)
- Safety Monitoring includes AEs, laboratory tests, ECG, vital signs

### Inclusion Criteria

- Age 18-85 years
- Treatment starts within 3-9 hours after onset of stroke symptoms
- Score of 4-20 on the NIHSS with clinical signs of hemispheric infarction suggestive of ischaemic stroke
- Distinct penumbra (at least 20%), measured by MRI (PWI/DWI) or perfusion CT



# Inclusion/Exclusion Criteria

## Inclusion criteria

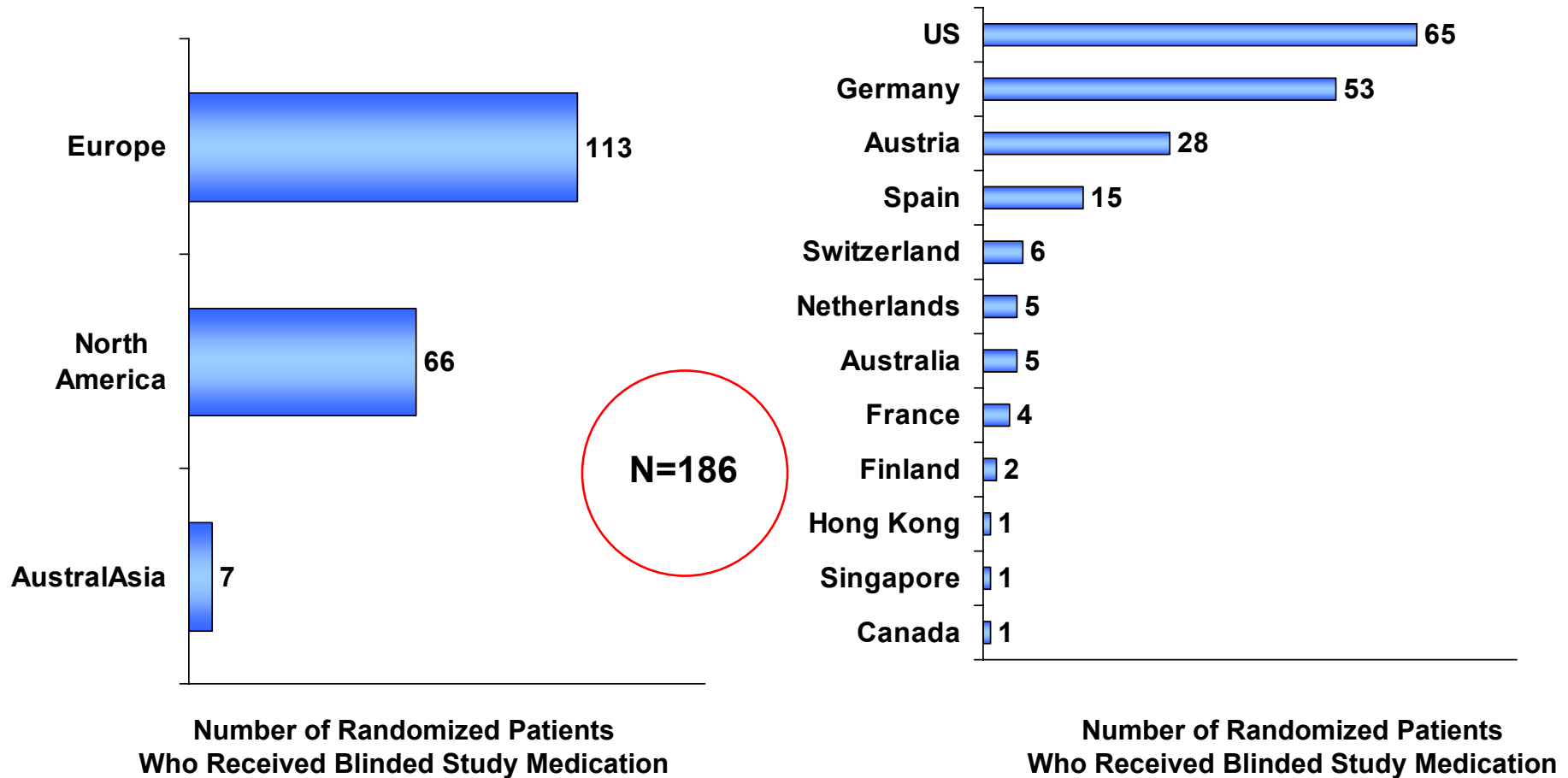
- Age 18-85 years
- Treatment within 3-9 hours after stroke onset
- Baseline NIHSS of 4-24
- $\geq 20\%$  salvageable ischemic tissue in MCA, ACA, or PCA territory as measured by imaging
  - PWI/DWI MR or perfusion CT

## Exclusion criteria

- Standard clinical exclusion criteria for thrombolytic trials
- Key imaging exclusions
  - Early infarction involving  $>1/3$  of MCA or entire ACA territory
  - Evidence of ICH or SAH, AV malformation, cerebral aneurysm, or cerebral neoplasm



# Patient Recruitment by Region and Country



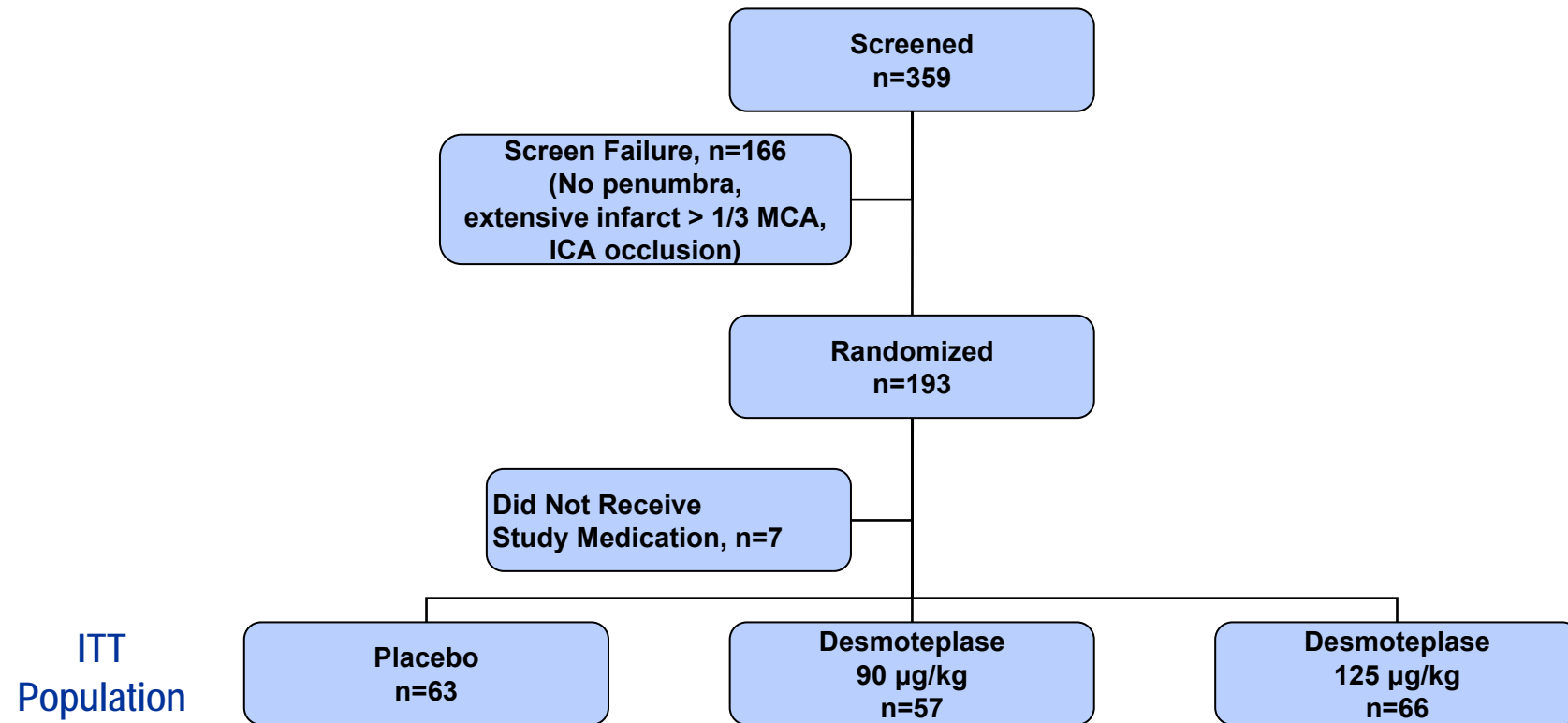


## Clinical Characteristics at Baseline

	Placebo n=63	Desmoteplase	
		90 µg/kg n=57	125 µg/kg n=66
NIHSS			
Median	9.0	9.0	9.0
Mean $\pm$ SD	10.3 $\pm$ 5.0	10.7 $\pm$ 5.6	10.4 $\pm$ 4.6
Time to treatment			
Mean $\pm$ SD (min)	391 $\pm$ 92	388 $\pm$ 88	402 $\pm$ 88
Diabetics			
n (%)	12 (19%)	16 (28%)	15 (23%)
Blood Pressure (mm Hg)			
systolic, Mean $\pm$ SD	156 $\pm$ 21	150 $\pm$ 22	152 $\pm$ 19
diastolic, Mean $\pm$ SD	84 $\pm$ 14	80 $\pm$ 12	81 $\pm$ 12



# Patient Disposition





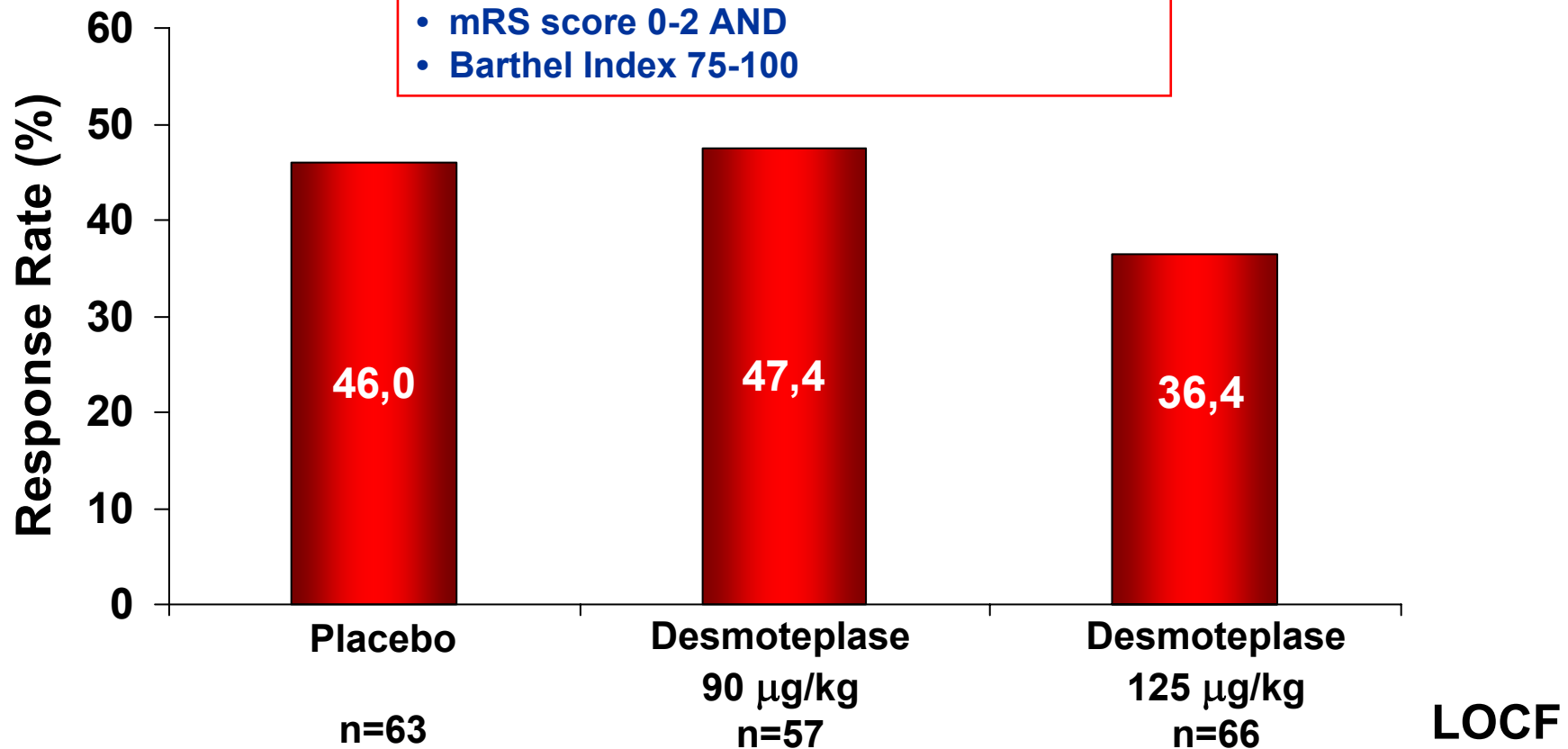
# Results

*ITT only*  
*per protocol in progress*

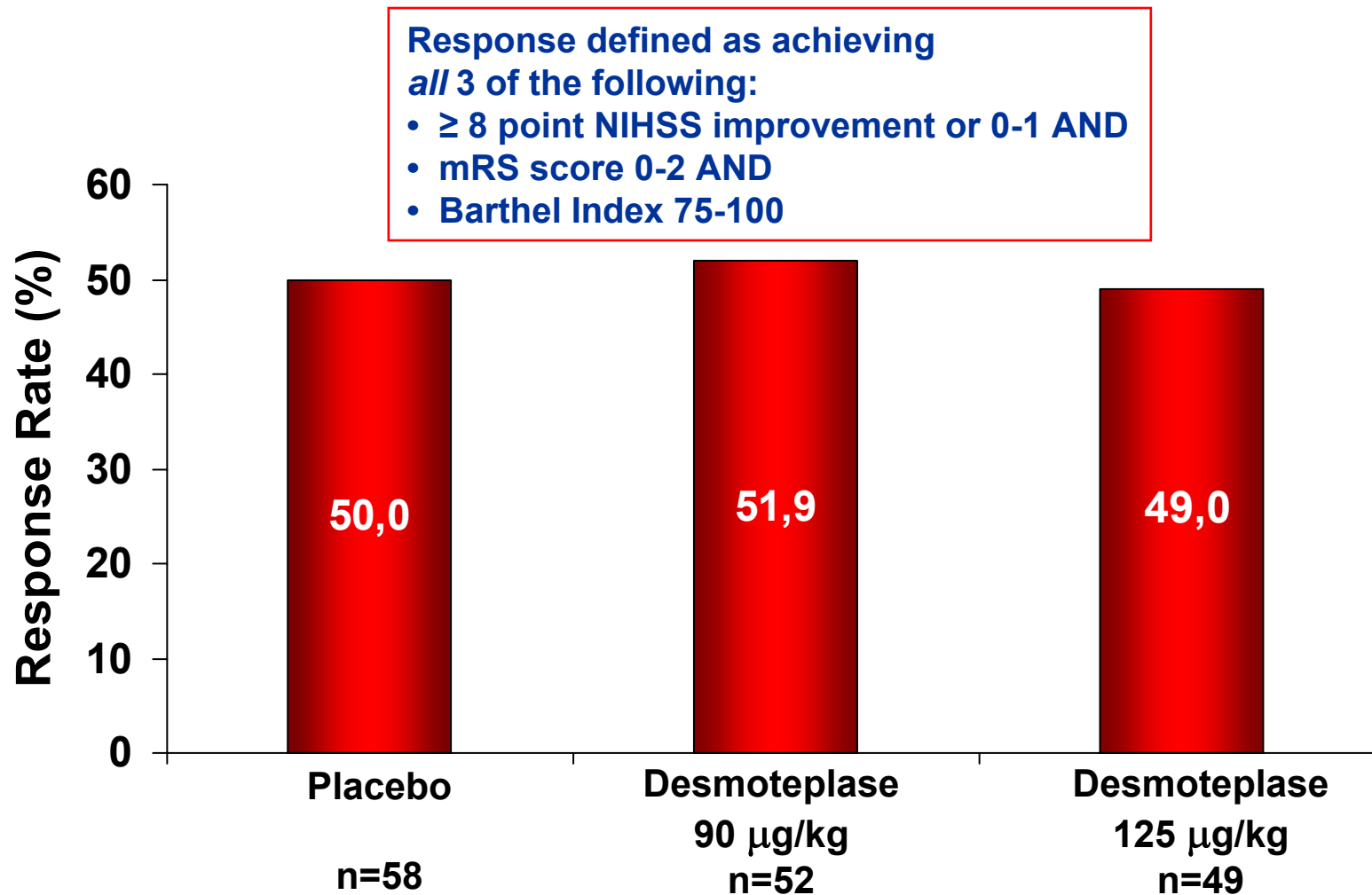
# Clinical Response at Day 90, ITT

Response defined as achieving *all 3* of the following:

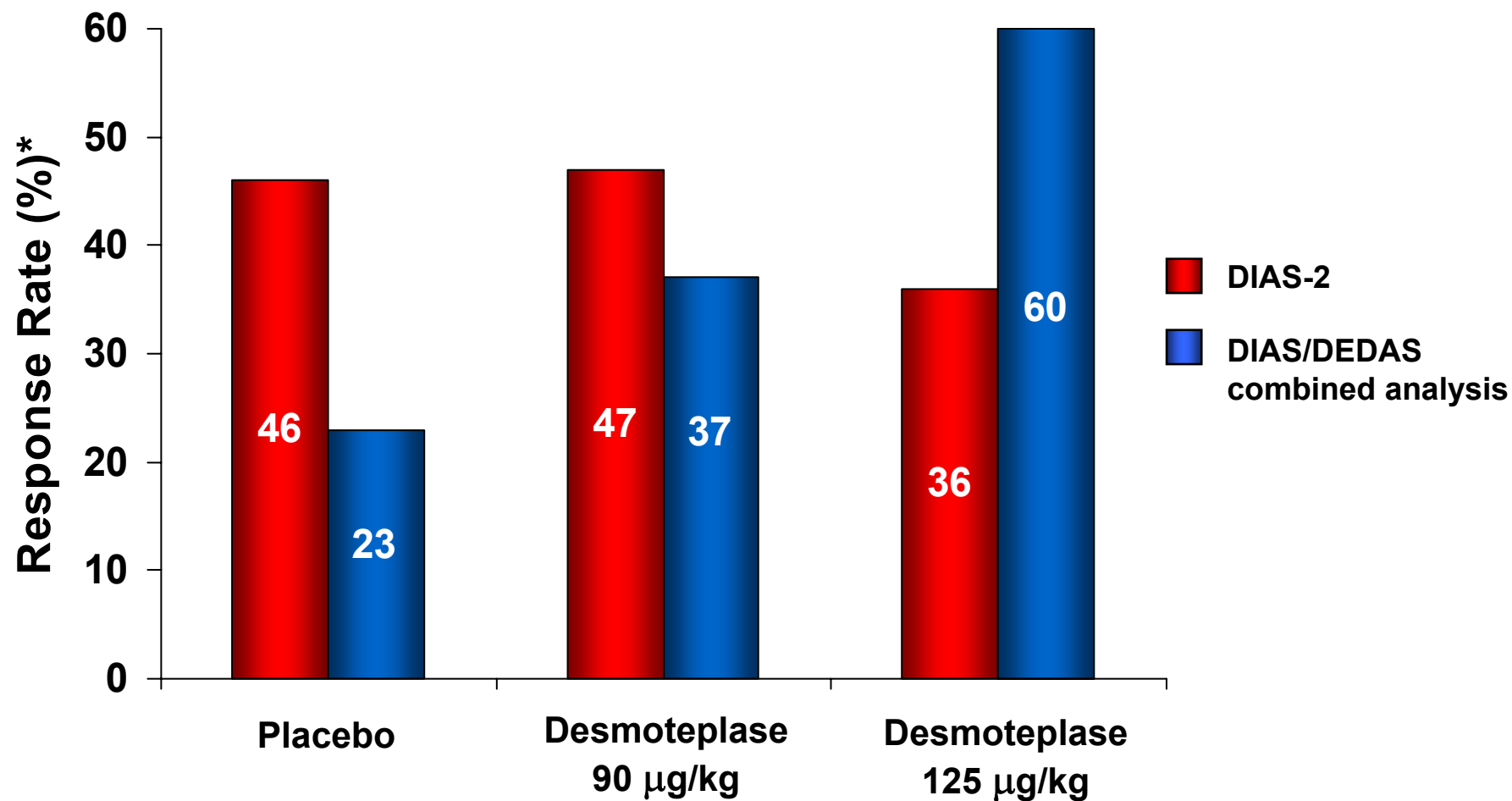
- $\geq 8$  point NIHSS improvement or 0-1 AND
- mRS score 0-2 AND
- Barthel Index 75-100



# Clinical Response at Day 90 without Dropouts



# DIAS-2 compared to DIAS/DEDAS



\* As defined previously



# Symptomatic ICH

	Desmoteplase		
	Placebo n=63	90 µg/kg n=57	125 µg/kg n=66
<b><i>sICH within 36 h</i></b>			
n (%)	0	2 (3.5%)*	2 (3.0%)
<b><i>sICH within 72 h</i></b>			
n (%)	0	2 (3.5%)*	3 (4.5%)

\* One patient had baseline ICH present prior to receiving study medication



## Other Safety Results

		Desmoteplase	
	Placebo n=63	90 µg/kg n=57	125 µg/kg n=66
<b><i>All-Cause 90-Day Death</i></b>			
n (%)	4 (6.3%)	3 (5.3%)	14 (21.2%)
<b><i>Major Systemic Bleeding</i></b>			
n (%)	1 (1.6%)	1 (1.8%)	1 (1.5%)



## Conclusions

- No significant difference in clinical outcome between desmoteplase and placebo
- Higher than expected placebo response rate
  - responder rate in placebo group as high as in desmoteplase groups
- Increased mortality in the 125  $\mu\text{g}/\text{kg}$  dose group
  - predominantly late death rate (>10 days)
- sICH rate is low in all treatment groups

## Next steps

- Exclusion of systematic errors in the study
- Understanding of the unexpectedly high response rate in the placebo group
- Further analysis
  - Patients with severe/mild strokes
  - Imaging techniques
  - Protocol violators
  - Effects by centres
- All 3 partners analyse independently
- Development of ideas for the next study

# Solid Financial Position

**Bernhard Hofer**  
**Chief Financial Officer**

Annual General Meeting  
Aachen, 20 June 2007



## Profit & loss statement

	FY 2005	FY 2006	Q1 2007
in k EUR			
Revenues	18,796	10,459	1,294
Cost of Revenues	-4,855	-7,252	-1,248
<b>Gross profit</b>	<b>13,941</b>	<b>3,207</b>	<b>46</b>
Research and development	-13,627	-16,487	-3,352
General and administrative	-4,852	-4,563	-1,013
Selling and Marketing	-1,370	-1,088	-208
Other income/expenses (net)	94	149	20
<b>Operating result</b>	<b>-5,814</b>	<b>-18,782</b>	<b>-4,507</b>
Financial result	1,058	1,396	341
<b>Net result</b>	<b>-4,756</b>	<b>-17,386</b>	<b>-4,166</b>
<b>Earnings per share (basic); in EUR</b>	<b>-0.31</b>	<b>-1.06</b>	<b>-0.25</b>

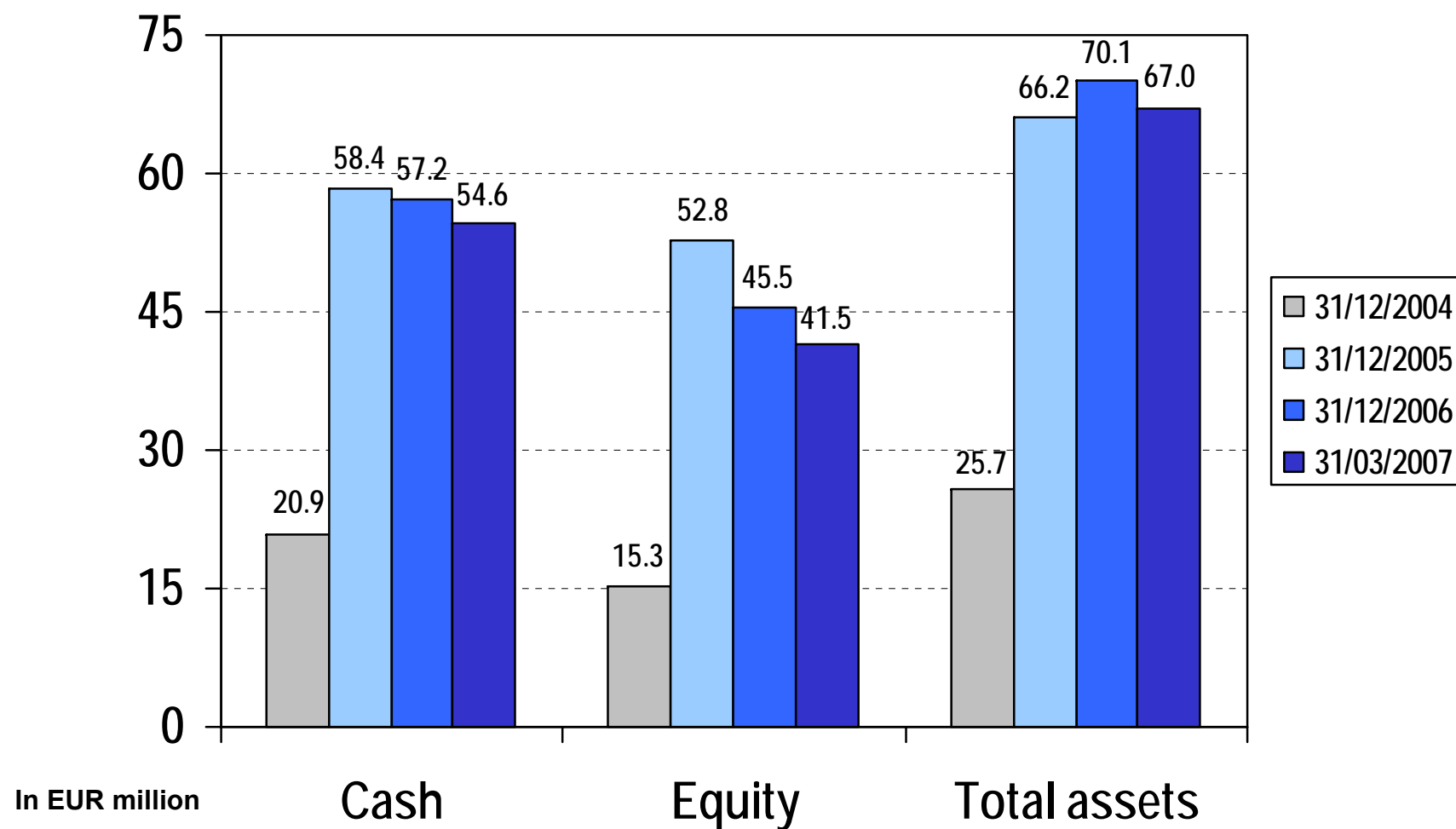
## Balance sheet - assets

in k EUR	12/31/2005	12/31/2006	03/31/2007
Non-current assets	5,282	9,699	10,727
<i>thereof: refund from Lundbeck</i>	3,674	8,011	9,044
Current assets	60,870	60,351	56,320
<b>Assets</b>	<b>66,152</b>	<b>70,050</b>	<b>67,047</b>

## Balance sheet – equity and liabilities

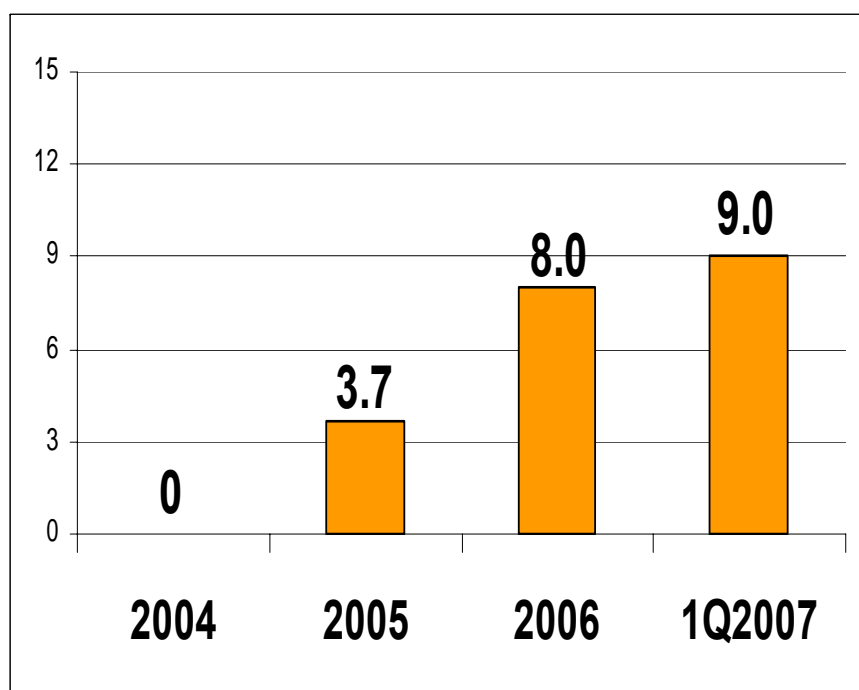
in k EUR	12/31/2005	12/31/2006	03/31/2007
Equity	52,750	45,471	41,541
Non-current liabilities	6,818	19,212	20,603
<i>therof obligation to Forest</i>	4,866	10,610	11,979
<i>thereof subordinated loan</i>	0	6,741	6,750
Current liabilities	6,584	5,367	4,903
<b>Equity and Liabilities</b>	<b>66,152</b>	<b>70,050</b>	<b>67,047</b>
<b>Equity ratio</b>			
a) Equity/Total assets	79.7%	64.9%	62.0%
b) (Equity + subordinated loan) / (Total assets - refund from Lundbeck)	84.4%	84.2%	83.3%

## Selected balance sheet items

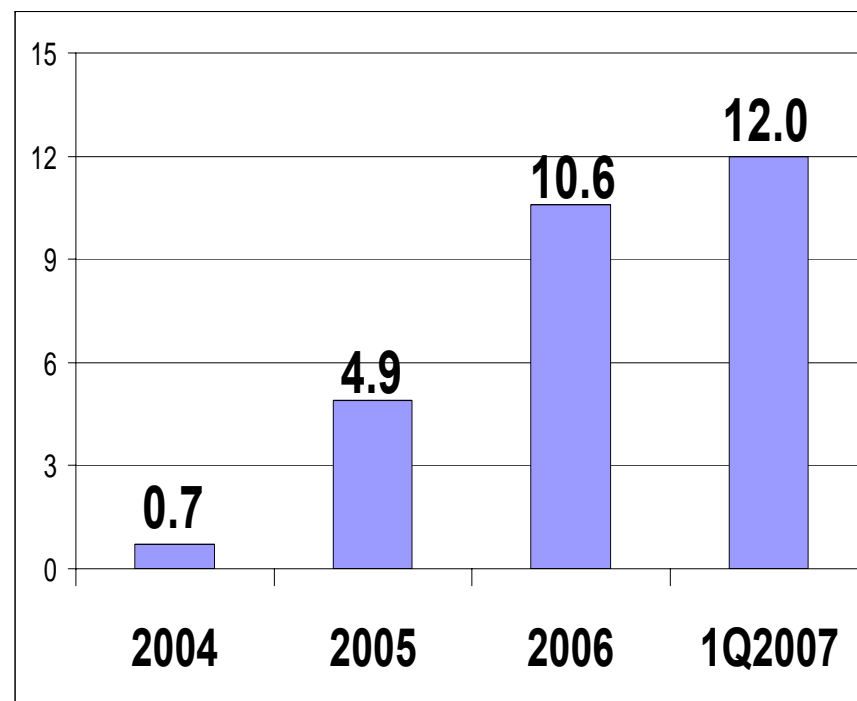


## Balance sheet illustration of the contracts with the cooperation partners

Long-term refund claim due from Lundbeck



Long-term obligation due to Forest



(in EUR million)

## Outlook 2007

- Significantly lower revenues than in 2006
  - Lower reimbursable development costs
  - No milestone payments expected in 2007 from Forest and Lundbeck
- Development of R&D expenses will mainly be driven by the decision of the cooperation partners and by PAION's decision on which development projects will be receive high priority
- Net loss as of 31 December 2007 (exact amount highly dependant on partners' decision)

## Note on the management board's report on sections 289 para. 4 and 315 para. 4 German Commercial Code

- Regarding the report of the Management Board to the statements in accordance with sections 289 para. 4, 315 para. 4 of the German Commercial Code reference is made to the statements of the Management Board in the annual report 2006 on the pages 36 to 39.

## Summary

- Solid equity position of EUR 41.5 million as of 31 March 2007
- Solid cash position of EUR 54.6 million as of 31 March 2007 ensures further ability to act
- If cooperations with Forest and Lundbeck maintain in place
  - Financing and development of Desmoteplase secured until ready for market
  - Outstanding milestones of up to EUR 80 million for indication of stroke until approval
  - Double-digit royalties or profit split after launch

# Strategic Options

Dr. Wolfgang Söhngen,  
Chief Executive Officer

Annual General Meeting  
Aachen, 20 June 2007



## Agenda

- **A short review of 2006**
- **Questions from shareholder's point of view**
- **Strategic options and next steps**

## Summary 2006

- Recruitment DIAS-2 completed
- Phase II Enecadin started
- Phase I Solulin postponed due to new regulatory requirements
- Expenses almost completely covered by a capital increase and a subordinate loan
- Solid financial position
- Shareholder basis expanded
- Broader analysts coverage

## Description of our situation

- Study results
- Financial position
- Close contact to cooperation partners
- Feedback from the investigators
- Feedback from shareholders

## Agenda

- A short review of 2006
- Questions from shareholder's point of view
- Strategic options and next steps

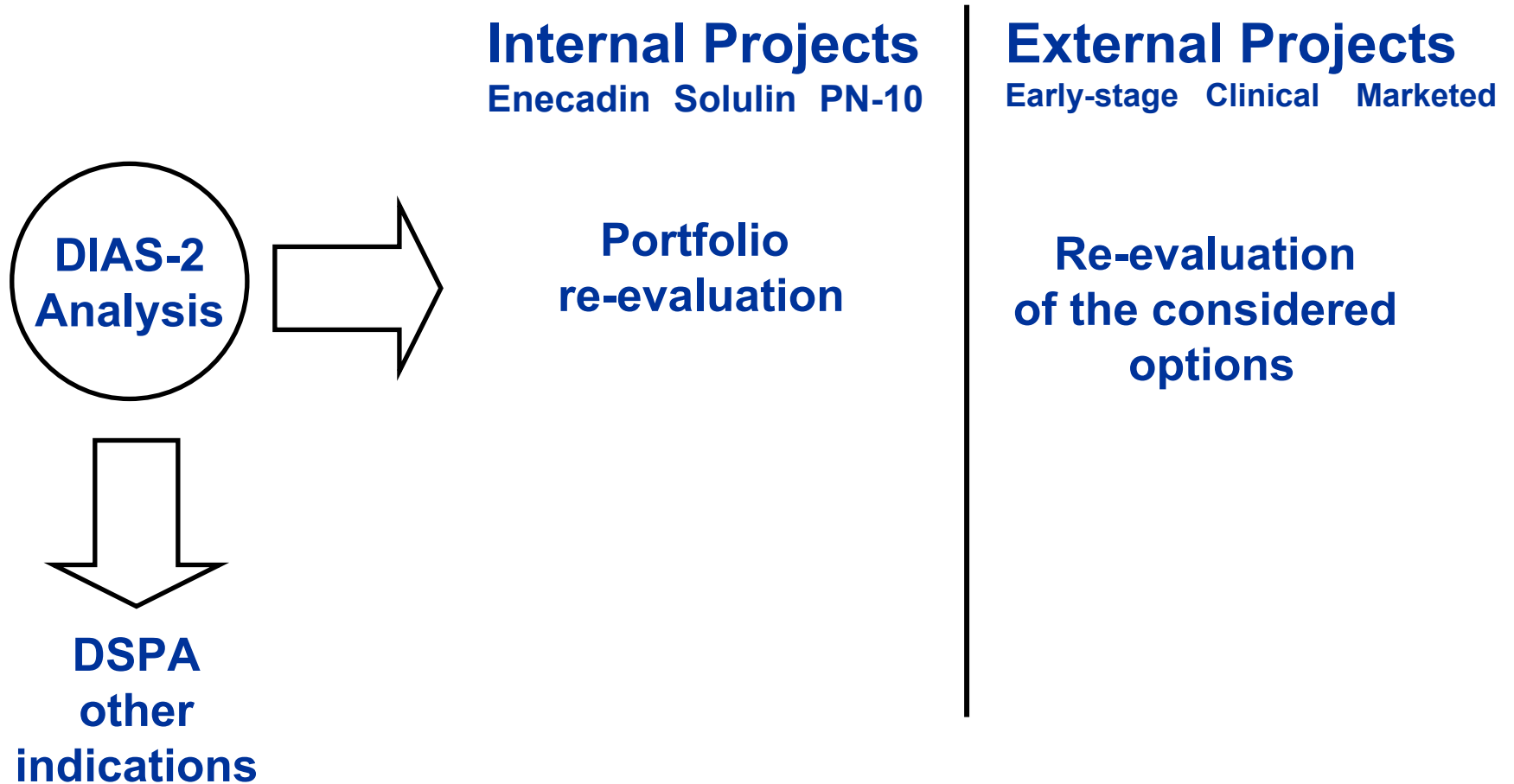
## Any news since Glasgow?

- Methods and extent of further analysis defined and initiated
  - To date no valid conclusions possible
  - Possible result: Another Phase III study
- ➔ A new study will most probably not be just a copy of DIAS-2

## How does PAION deal with the DIAS-2 results?

- Management has always taken all possible scenarios into consideration in their planning
- In the budget 2006/2007 cost relevant decision were intentionally planned for the time after presentation of the results
- The management has prepared an action plan which aims at reducing internal and external cost effectively and which should be in place on a short notice
- In parallel: Analysis of further strategic options

## Strategy process



## When do partners decide how to continue?

- The results of DIAS-2 are currently being analysed in detail together with the two partners
- The results of this in-depth analysis will build the decision basis for the partners
- Time schedule

## Engagement of the partners after the DIAS – 2 results

- Both partners invest in the detailed analysis of the data
- The partner teams fight for the project
- But: What happens if one or both partners decide to end the cooperation?
  - Desmoteplase is continued with a new (co-) sponsor
  - Desmoteplase is discontinued in stroke
  - Decision on alternative indications

## Status of the pipeline

### a) Desmoteplase – evaluation of new indications

- Attractivity for PAION can not be judged yet finally
  - compared to stroke
  - in relation to necessary investments (study size, observation time, dose, competition)

### b) Enecadin – makes more sense with Desmoteplase than without

- Market size determined by reperfusion therapies
- Re-evaluation after completion of the first dose tier of the TEST study planned
  - Alternative indications are also being evaluated

## Status of the pipeline

### c) Solulin – potential identified also for indications not connected to stroke

- In 2006/2007 further pre-clinical studies have been conducted which confirmed the attractiveness of the substance and support a positioning in other indications than stroke
- Phase I is expected to start in Q4/2007 at latest after meeting the new regulatory requirements in the EU
- Phase II indication will be decided after Phase I results are available; out-licensing Solulin could be considered after completion of Phase IIa

## Agenda

- **A short review of 2006**
- **Questions from shareholder's point of view**
- **Strategic options and next steps**

## Strategic options

- Desmoteplase is the major asset in the pipeline
- Re-positioning of internal projects
- Explore further indications parallel to stroke
- Consideration of external projects

## Next steps

- Complete detailed analysis of the DIAS-2 results
- Integrate the decision of the partners into the PAION strategy
- Re-evaluation of the pipeline products in context of the partners' decision
- Reduction of external and internal costs
- Prioritise external projects

## PAIONs strengths – future opportunities

- Cash
- Listing
- Infrastructure
- Management
- Product pipeline
- Proof of concept for DSPA in 3 indications
- Track Record
  - Clinical Development
  - Transactions (Bus. Dev.)
  - Finance (private/public)
  - Production management
  - (Pre-) Marketing
  - Products (IP, know-how)
  - Global network
- Attractive partner for companies without development infrastructure