

## Cautionary Statement Regarding Forward-Looking Statements



In order to utilise the 'Safe Harbor' provisions of the United States Private Securities Litigation Reform Act of 1995, AstraZeneca is providing the following cautionary statement. This presentation contains forward-looking statements with respect to the financial condition, results of operations and businesses of AstraZeneca. By their nature, forward-looking statements and forecasts involve risk and uncertainty because they relate to events and depend on circumstances that will occur in the future. There are a number of factors that could cause actual results and developments to differ materially from that expressed or implied by these forward-looking statements. These factors include, among other things, the loss or expiration of patents, marketing exclusivity or trade marks; exchange rate fluctuations; the risk that R&D will not yield new products that achieve commercial success; the impact of competition, price controls and price reductions; taxation risks; the risk of substantial product liability claims; the impact of any failure by third parties to supply materials or services; the risk of delay to new product launches; the difficulties of obtaining and maintaining governmental approvals for products; the risk of failure to observe ongoing regulatory oversight; the risk that new products do not perform as we expect; and the risk of environmental liabilities.

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Neuroscience:  
Early development portfolio

Ihor Rak

## 1990s was the “decade of the brain”



### New, better quality targets

- Diseases previously thought untreatable now offer viable approaches
  - Alzheimer's
- Possibility of “breakthrough” levels of efficacy in some conditions

### More reliable drug development

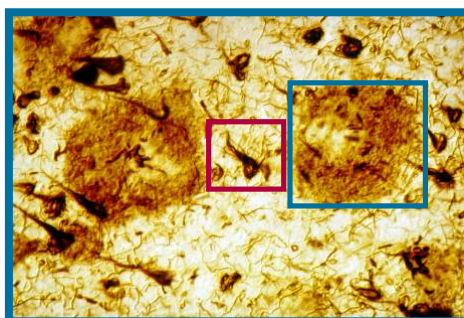
- PET and functional imaging allow reliable dose choices for clinical development
- Validated human disease-models and biomarkers show efficacy early in clinical development

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## New, better quality targets



### Alzheimer's disease pathology



Amyloid plaque

Neurofibrillary tangles  
NFTs

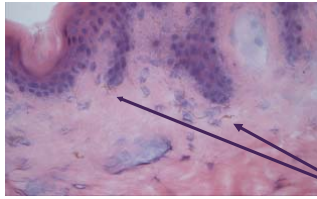
AZ has approaches in development for both of these pathologies

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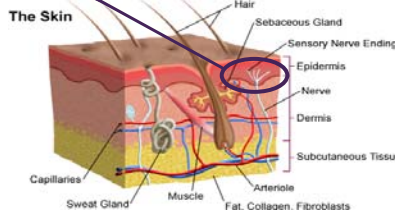
# New, better quality targets



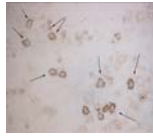
## Genomics in practice



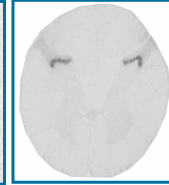
Epidermis  
Dermis



Human DRG



Radioligand binding



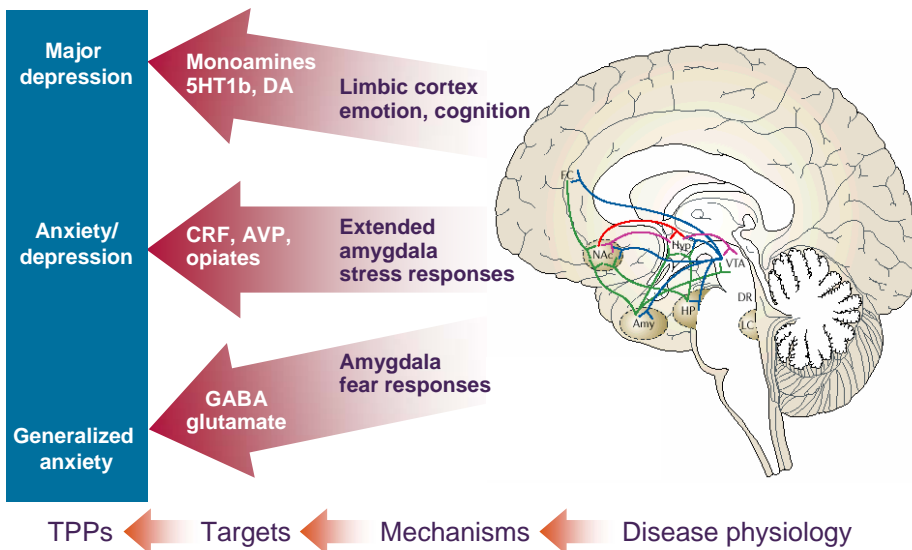
Immuno - histochemistry

Human spinal cord

Human specific targets strongly related to pain pathways

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# New, better quality targets



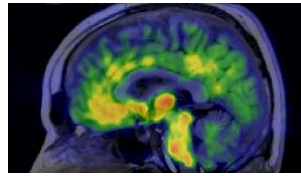
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## More reliable drug development

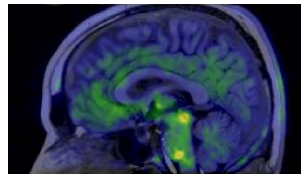


**Predict  
the  
right  
dose!**

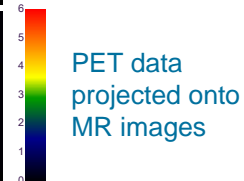
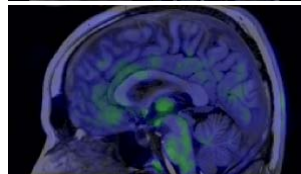
Baseline



X mg



1.5 x X mg



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## A rich Neuroscience pipeline with strong progression in the last 12 months



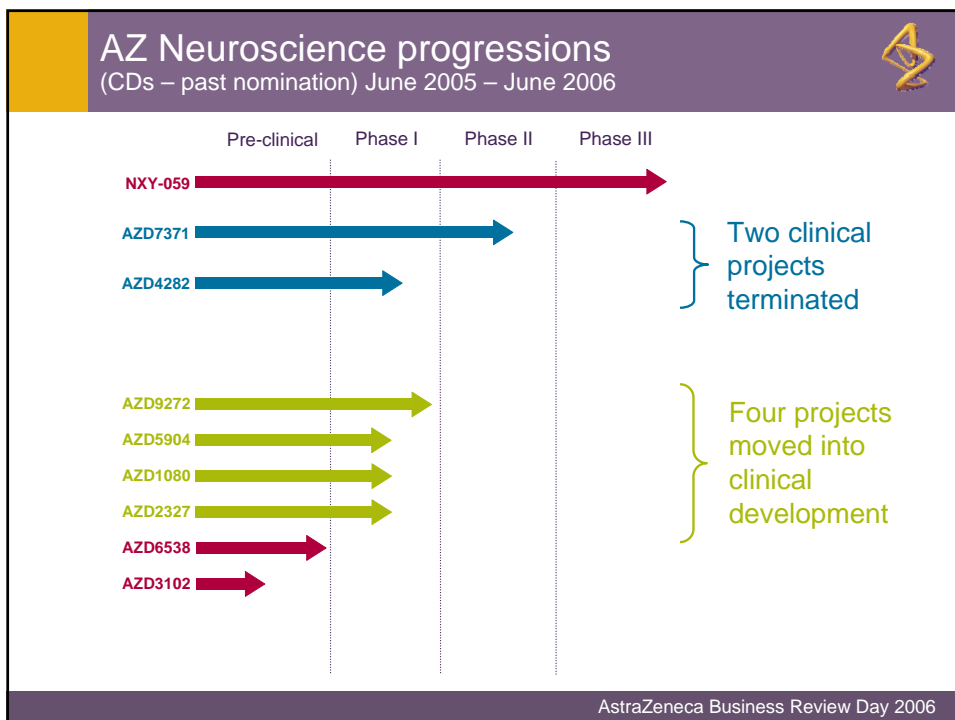
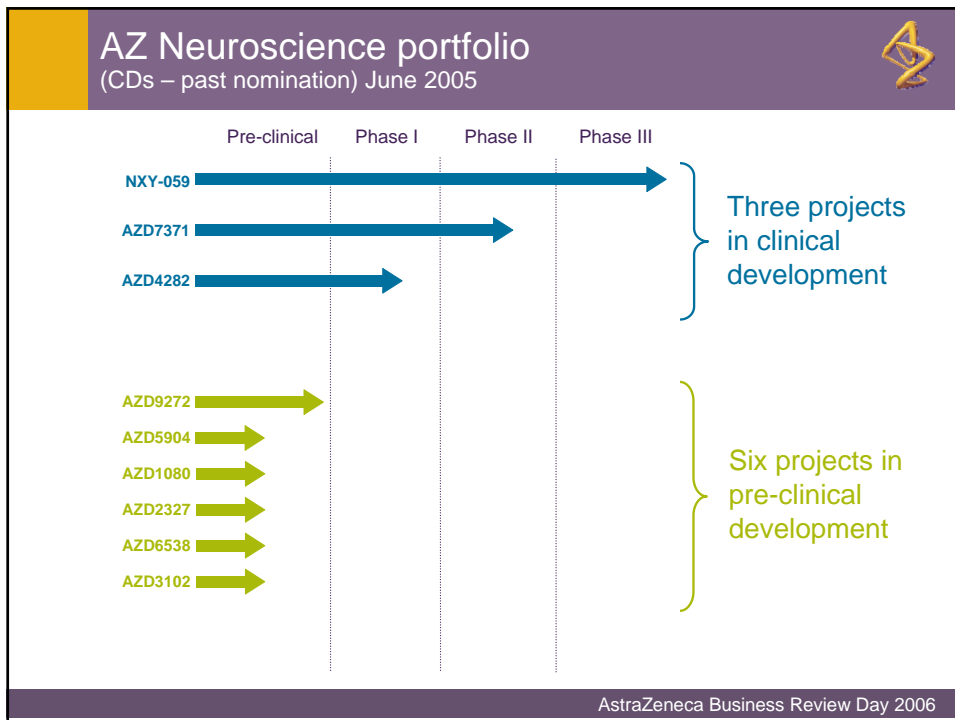
### Progressions

- Seven new molecules into preclinical development
- Four molecules enter clinical phase I
  - three in first half of 2006
- One in-licensed compound enters phase II

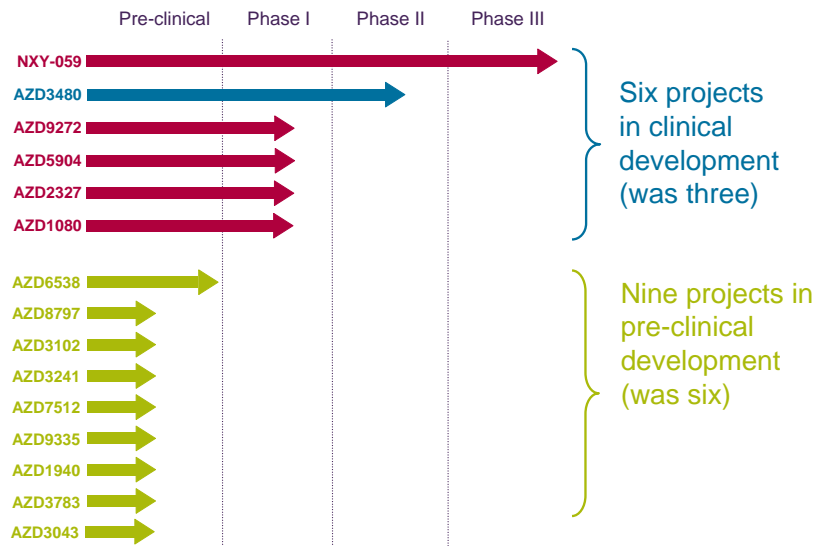
### Discontinuations

- Two “efficient closures” for failure to achieve TPP
  - AZD7371 and AZD4282

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## AZ Neuroscience portfolio (CDs – past nomination) June 2006

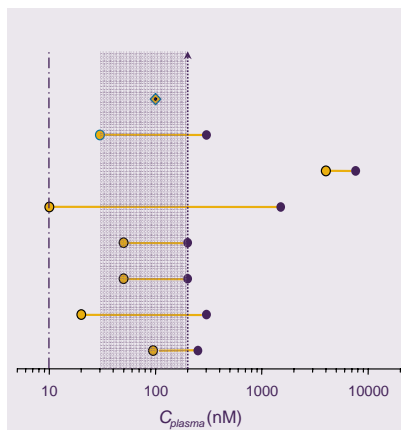


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## AZD9272: glutamate receptor modulator for refractory pain

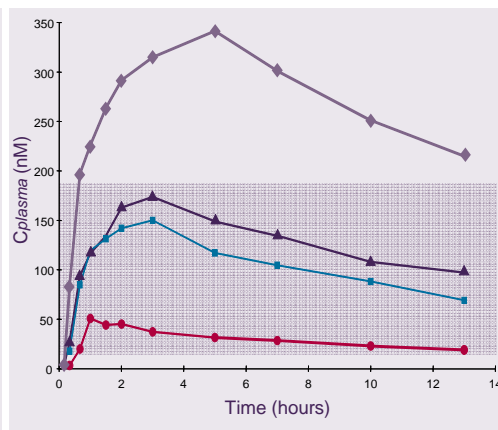


### Pharmacological effects in animals



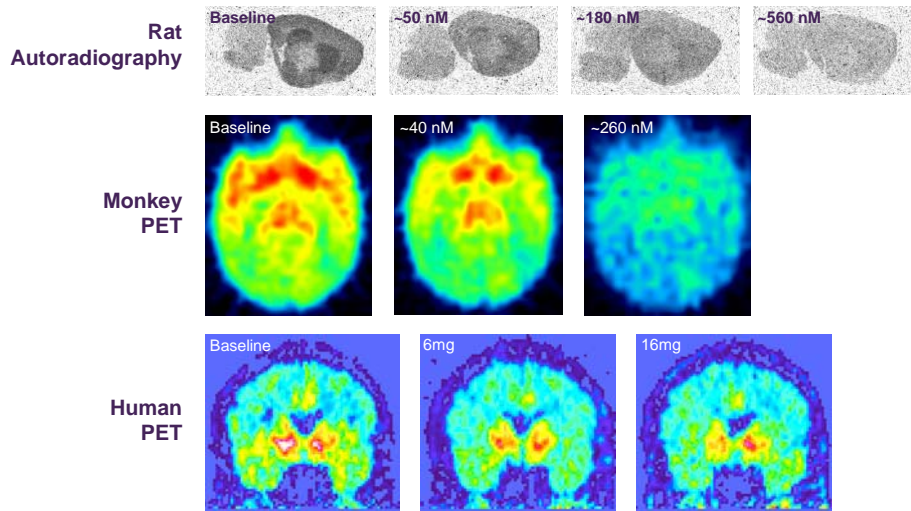
- Minimum significant effect
- Maximum possible effect

### Human exposure



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## AZD9272: Receptor occupancy from rat to man

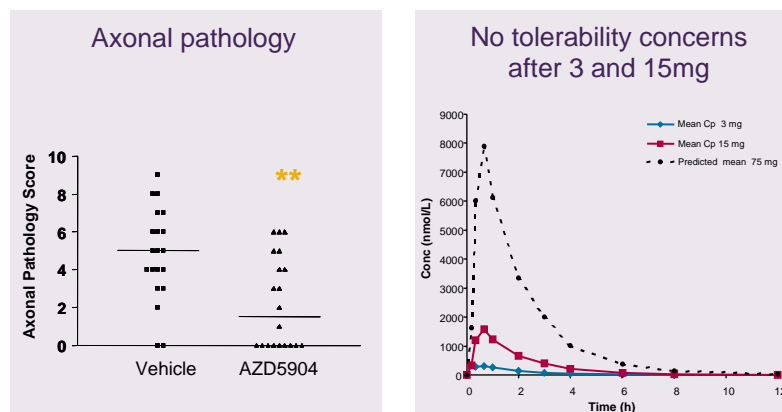


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## AZD5904: Enzyme inhibitor for neurodegenerative diseases

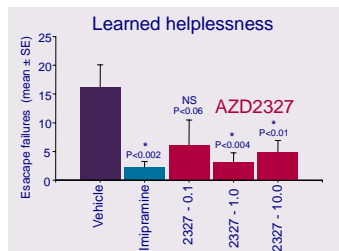
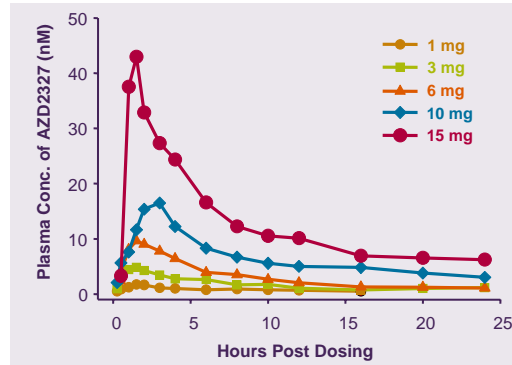
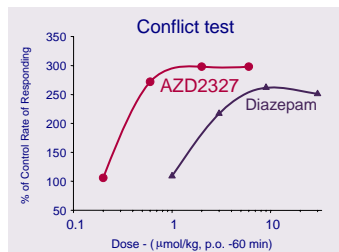


Effect of AZD5904 in mouse EAE compared to plasma concentrations in man



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## AZD2327 enkephalinergic receptor modulator for anxiety and depression

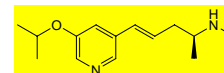


Effective in animal models at 4nM

No safety and tolerability concerns at those concentrations after single doses in man

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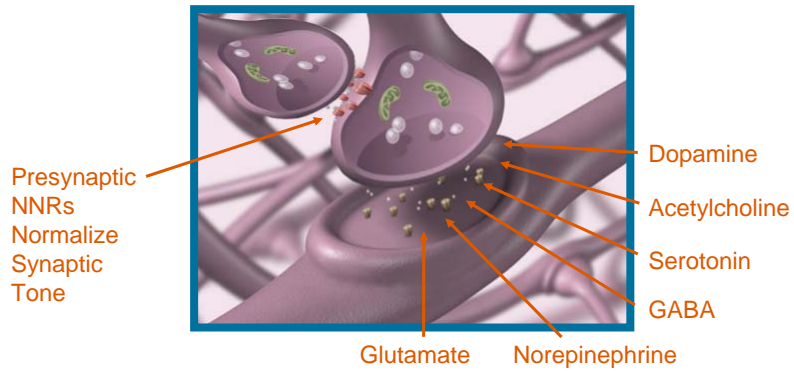
## Targacept neuronal nicotinic receptor agents



- AZD3480
  - Highly selective  $\alpha 4\beta 2$  neuronal nicotinic receptor agent (SNNRA)
  - Successfully completed phase II trials in memory impaired subjects
  - Clinical phase II trials planned for treatment of Alzheimer's disease and cognitive deficits associated with schizophrenia (CDS), future trials contemplated for other conditions of cognitive dysfunction
  - AZ to develop, manufacture and commercialise
  - Staged payments and royalties
- R&D collaboration for four follow-on CDs
- Rights for CDs offered by Targacept with alternative NNR mechanisms

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## Stimulation of Neuronal Nicotinic Receptors (NNRs) improves cognition



Phase II studies in > 250 subjects with memory impairment treated with AZD3480 consistently show improved attention, episodic memory and speed of memory

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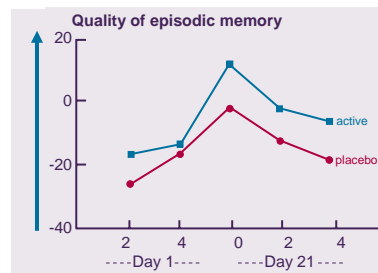
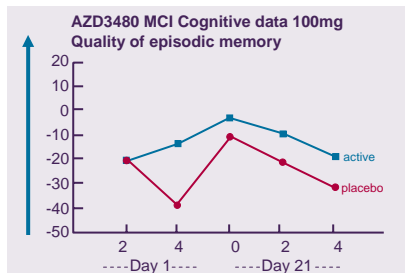
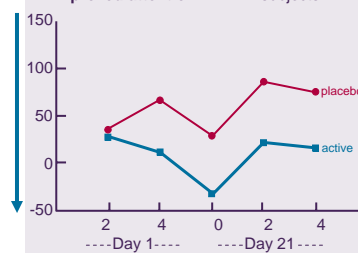
## AZD3480: Efficacy in memory impaired subjects



### AZD3480 efficacy signals (P<0.05)

	Power of attention	Continuity of attention	Episodic memory	Working memory	Speed of memory
50 mg AAMI n=20	✓	✓	✓		✓
100 mg AAMI n=20	✓		✓		
50 mg MCI N=19					✓
100 mg MCI N=17	✓		✓		

### Improved attention in AAMI subjects



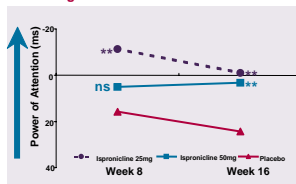
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## AZD3480: AAMI clinical efficacy

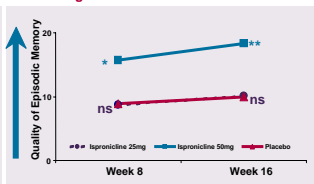


	Primary Endpoints			Secondary			SGI Subscores		
	Power of attention	Quality of episodic memory	Subject global impression (SGI)	Speed of memory	Quality of working memory	Continuity of attention	Attention improvement	Quality of working memory	Speed of memory
50 mg AAMI N = 68	✓	✓	✓	✓	✓		✓	✓	✓
25 mg AAMI N = 59	✓			✓		✓			

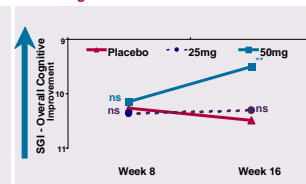
Change from baseline at weeks 8 & 16



Change from baseline at weeks 8 & 16



Change from baseline at weeks 8 & 16



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## AZD3043 (TD-4756): A novel IV short acting anaesthetic licensed from Theravance Inc.



### Territory and scope

- Exclusive global license to develop, manufacture and commercialise

### What is AZD3043?

- Positive allosteric GABA-A receptor modulator
- Currently in pre-clinical development

### Potential development indications

- Induction and maintenance of anaesthesia
- Sedation for short term surgical and diagnostic procedures
- ICU sedation

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## Neuroscience summary



- Important therapeutic area – significant market growth through fulfilling unmet medical need
- New technologies such as imaging ensure robust clinical development programmes
- Major enrichment of pipeline through harvesting previous internal investment and licensing and acquisitions
  - Eight new molecules in development
  - Five exciting new molecules in clinical testing
    - One in-licensed opportunity directly into phase II

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