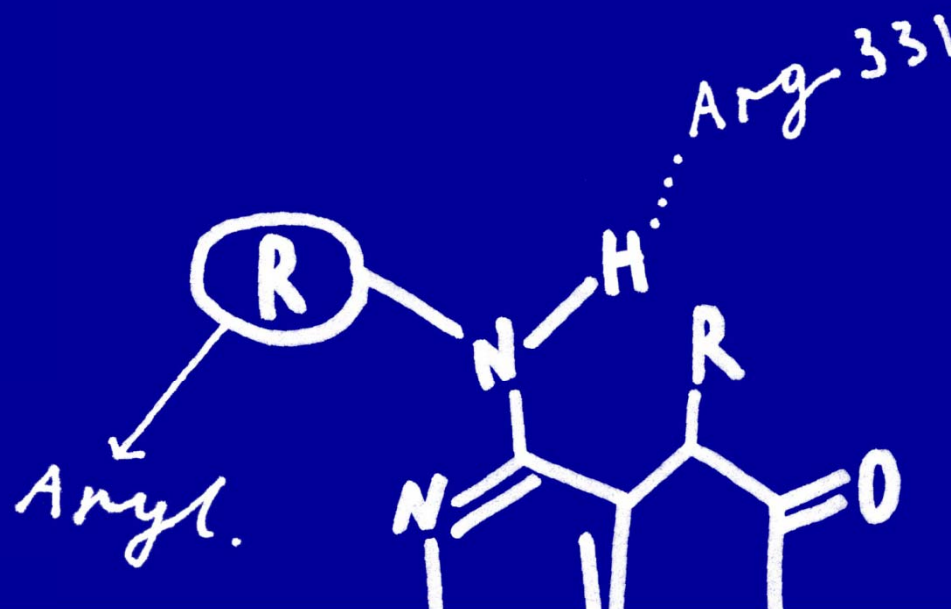


---

Evotec & Roche

# MAO-B inhibitor for development in Alzheimer's Disease



## Forward-looking statement

---

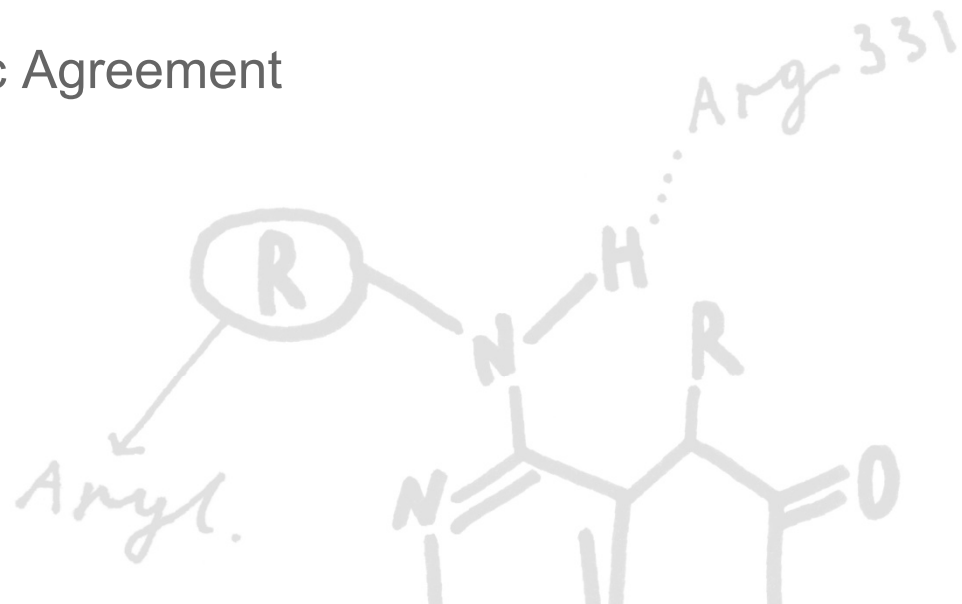
*Information set forth in this presentation contains forward-looking statements, which involve a number of risks and uncertainties. The forward-looking statements contained herein represent the judgement of Evotec as of the date of this report. Such forward-looking statements are neither promises nor guarantees, but are subject to a variety of risks and uncertainties, many of which are beyond our control, and which could cause*

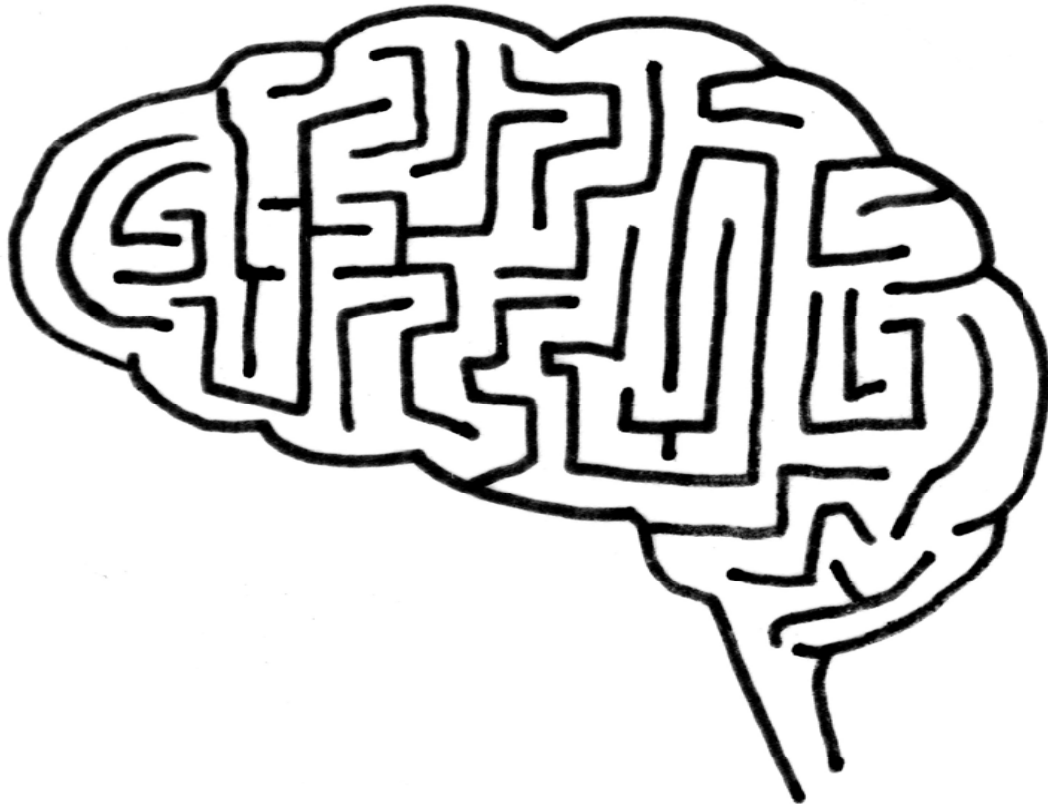
*actual results to differ materially from those contemplated in these forward-looking statements. We expressly disclaim any obligation or undertaking to release publicly any updates or revisions to any such statements to reflect any change in our expectations or any change in events, conditions or circumstances on which any such statement is based.*

## Agenda

---

- **Summary and Highlights**
- Market Opportunity
- MAO-B Inhibitors in Alzheimer's Disease (AD)
- Competitive Landscape
- The Roche-Evotec Agreement





***“I now begin the  
journey that will lead  
me into the sunset of  
my life”***

***(from Ronald Reagan's letter to the  
American people concerning his  
diagnosis of Alzheimer disease)***

# One of the largest efforts to fight Alzheimer's disease

---




## Summary & Highlights

---

<b>The Goal</b>	<ul style="list-style-type: none"><li>• Development of MAO-B inhibitor to slow down progression in Alzheimer's disease (AD)</li></ul>
<b>The Agreement</b>	<ul style="list-style-type: none"><li>• Upfront payment of \$10 million</li><li>• Development milestone payments of up to \$170 million</li><li>• Commercial milestone payments of up to \$ 650 million</li><li>• Tiered double-digit royalties on net sales</li></ul>
<b>Next Steps</b>	<ul style="list-style-type: none"><li>• Roche will initiate a 12 months treatment Phase IIb study in 2012 to demonstrate proof-of-concept prior to a pivotal Phase III</li><li>• All development and commercialization costs funded by Roche</li></ul>

# Roche the ideal partner for AD development

## Portfolio of product development partnerships

Indication	Partner	Status	Upside for Evotec	Next milestone
Type 1 diabetes <sup>1)</sup>	 	Phase III	+++	Phase III data 2012
<b>Alzheimer's Disease</b> 		Phase II	+++++	Phase IIb initiation
Treatment resistant depression (TRD)	open	Phase II	+++	New partnering initiative
Insomnia <sup>2)</sup>		Phase II	++	Phase IIb data 2012
Pain		Phase I	++	Phase I
Inflammatory diseases	Animal Health (undisclosed)	Phase I/II	+++	Phase II start in 2012
CNS; Pain, UI, others <sup>3)</sup>	open	Pre-clinical	+++	Phase I / partnering

1) DiaPep277 is being developed by Andromeda Biotech Ltd and has been partnered with TEVA Pharmaceuticals Industries Ltd

2) Chinese rights only; Safety and Phase IIb study planned starting 2011

3) EVT 501(H3), P2X3, EVT 401 (P2x7), ...

# One time effect leads to further increased revenue guidance

## Updated operational business overview

In € m	Old guidance 2011	New guidance 2011	FY 2010
Revenues	70 -72 <sup>1)</sup>	77–79 <sup>2)</sup>	55.3
Operating Income	Improved over 2010	Improved over 2010	1.7
Net Income	Improved over 2010	Improved over 2010	3.0
Unpartnered R&D expenses	Approx. 10	Approx. 10	6
Liquidity at period end	55 <sup>1) 3)</sup>	Above 60 <sup>3)</sup>	70

1) Original guidance of € 64 m– € 66 m revenues and € 65 m cash was changed after acquisition of Compound Focus, Revenue guidance was raised after H1 results to €70 – 72m

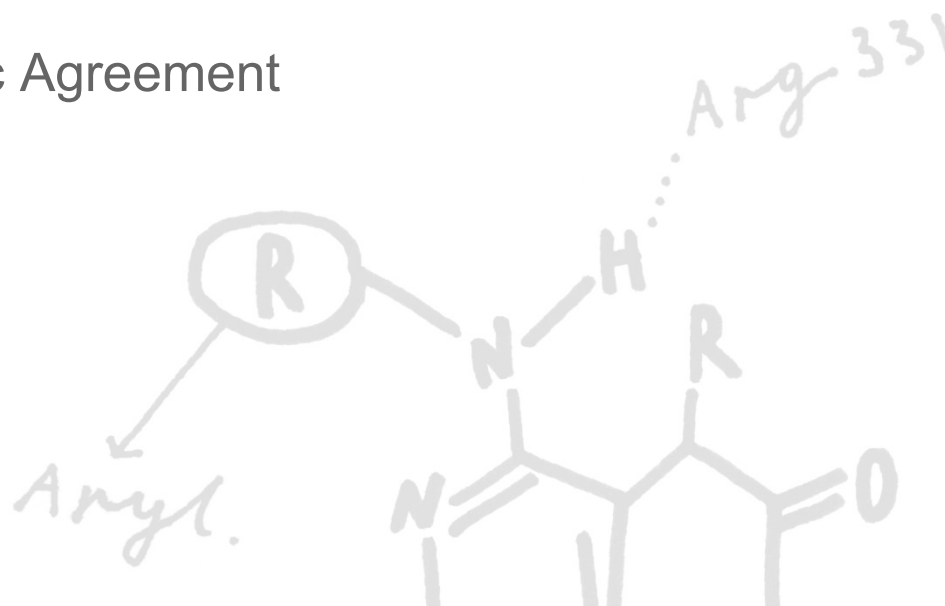
2) USD 10 m upfront payment will be recognized in 2011; but should be seen as a ONE TIME effect

3) Including cash acquisition payments to Galapagos and Kinaxo shareholders and earn-out payments in respect of Kinaxo and DeveloGen

## Agenda

---

- Summary and Highlights
- **Market Opportunity**
- MAO-B Inhibitors in Alzheimer's Diseases (AD)
- Competitive Landscape
- The Roche-Evotec Agreement

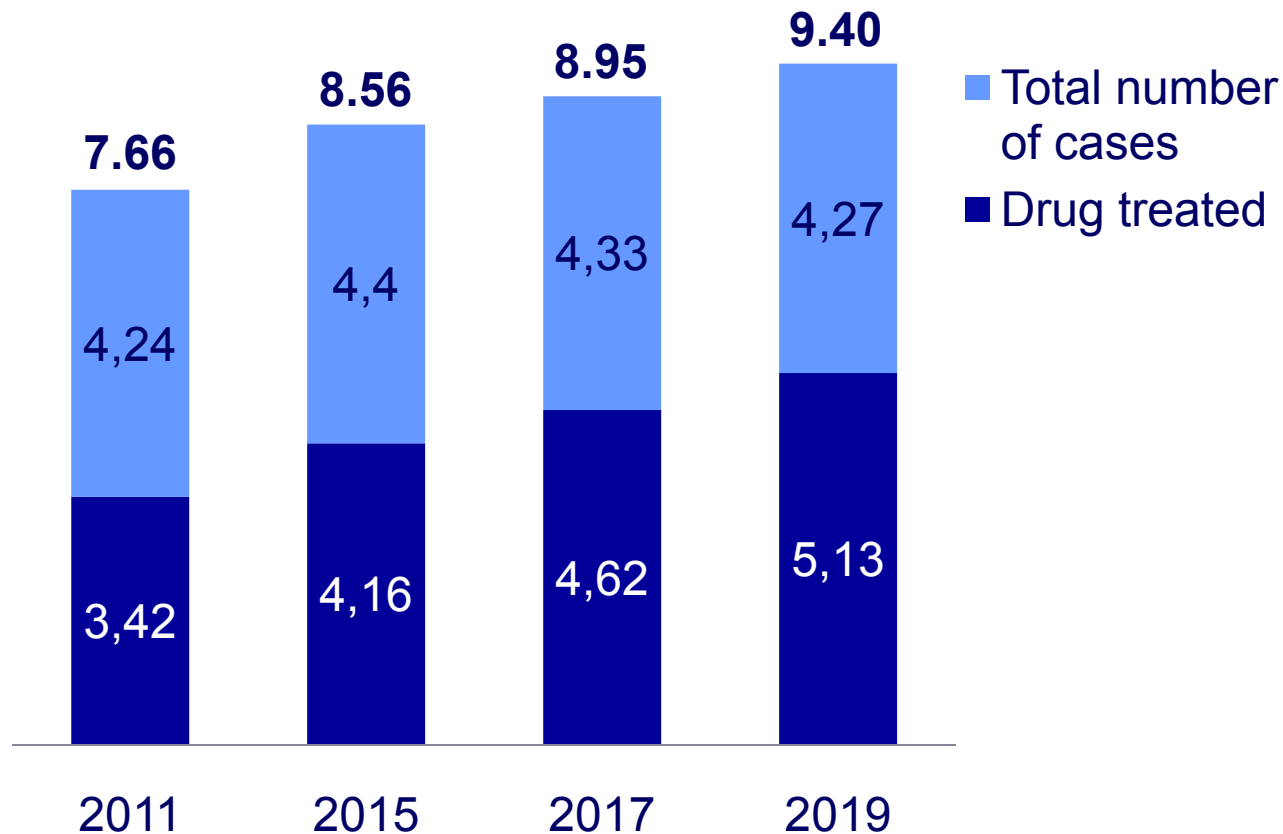




# A dramatically growing unmet medical need

Total and Drug-Treated Cases of Alzheimer's Disease 2011-2019<sup>1)</sup>

in Mio.



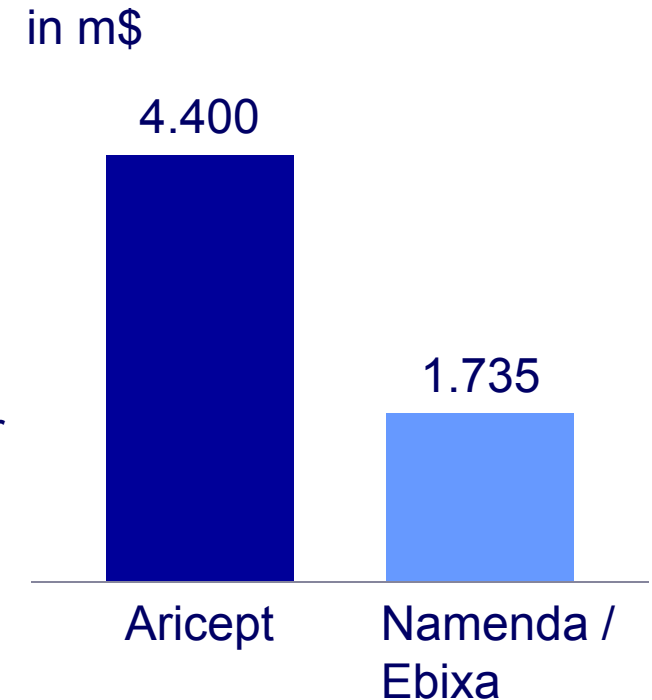
## Huge market opportunity for any new therapy driven by growing patient population

- Number of Alzheimer's Disease patients increases dramatically
- Increasing diagnosis rate
- In only the seven major markets, there will be over 9 M prevalent cases of AD in 2019

# Current treatments of AD show only a short term symptomatic effect

## Market overview

- Only two classes of drugs approved for AD
  - Market dominated by acetylcholine esterase inhibitor Aricept (Pfizer/Eisai) and NMDA antagonist Namenda/Ebixa (Forest/Lundbeck)
  - Combined sales of over \$ 5 BN despite limited efficacy
- Major unmet medical need remains
  - Agents which modify course of the disease and provide greater slowing of functional decline
  - Large opportunity due to low attainment of unmet needs
  - Total market size of over \$ 13 BN for Alzheimer’s Disease therapies by 2019

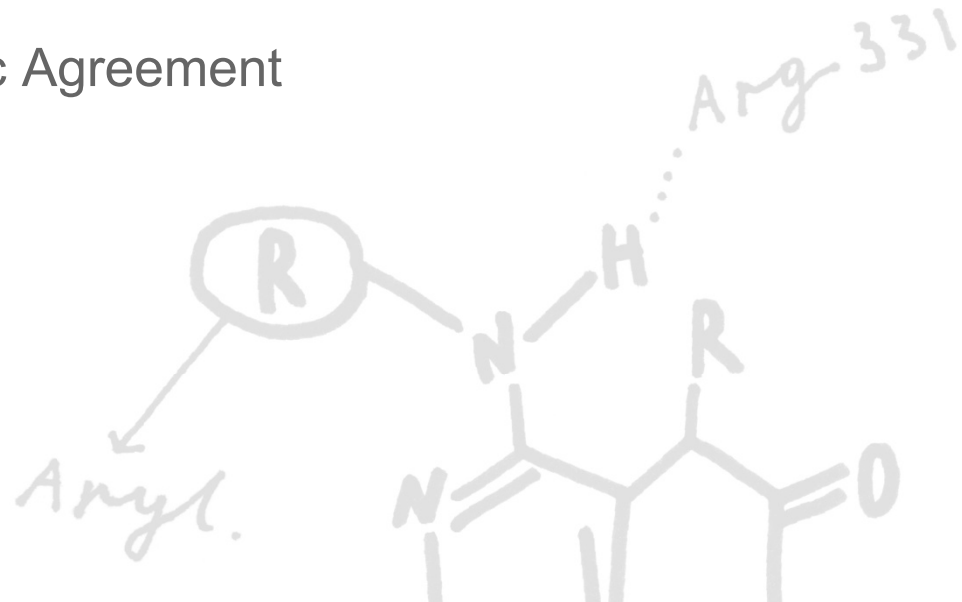


**Because of limited efficacy new treatments are desperately needed**

## Agenda

---

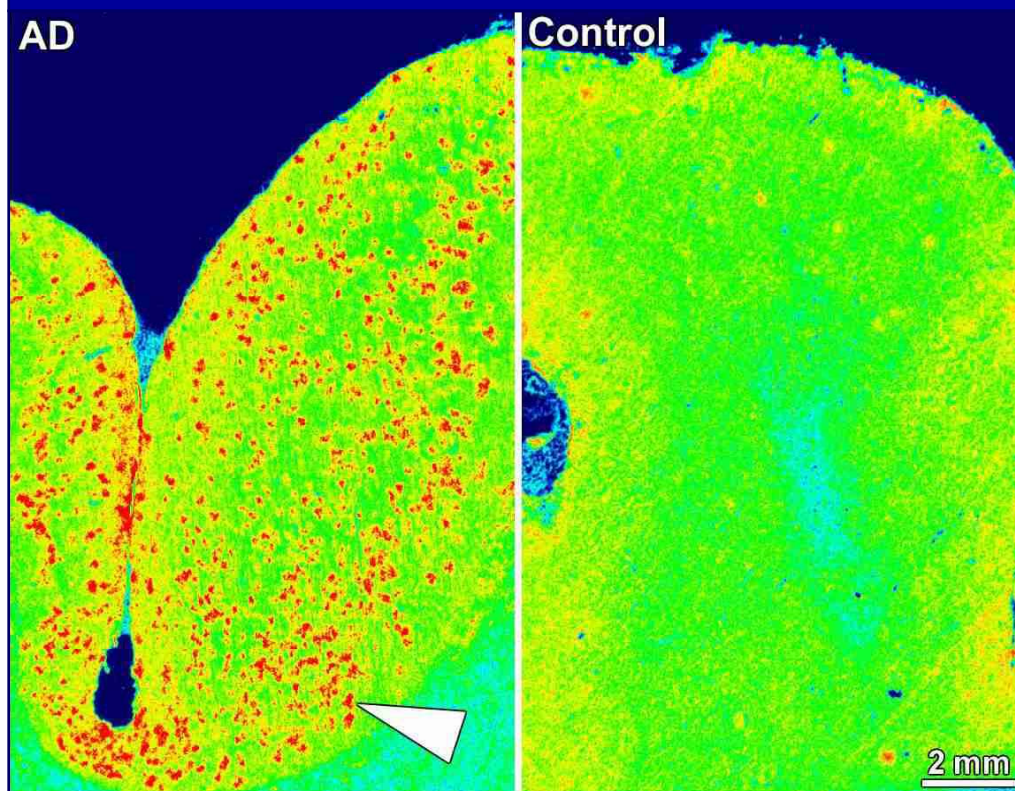
- Summary and Highlights
- Market Opportunity
- **MAO-B Inhibitors in Alzheimer's Diseases (AD)**
- Competitive Landscape
- The Roche-Evotec Agreement



# MAO-B is over-expressed in brains of AD patients - Activity may contribute to neurodegeneration

## MAO-B Mechanism of action

### MAO-B expression in AD patient post-mortem brain <sup>1)</sup>



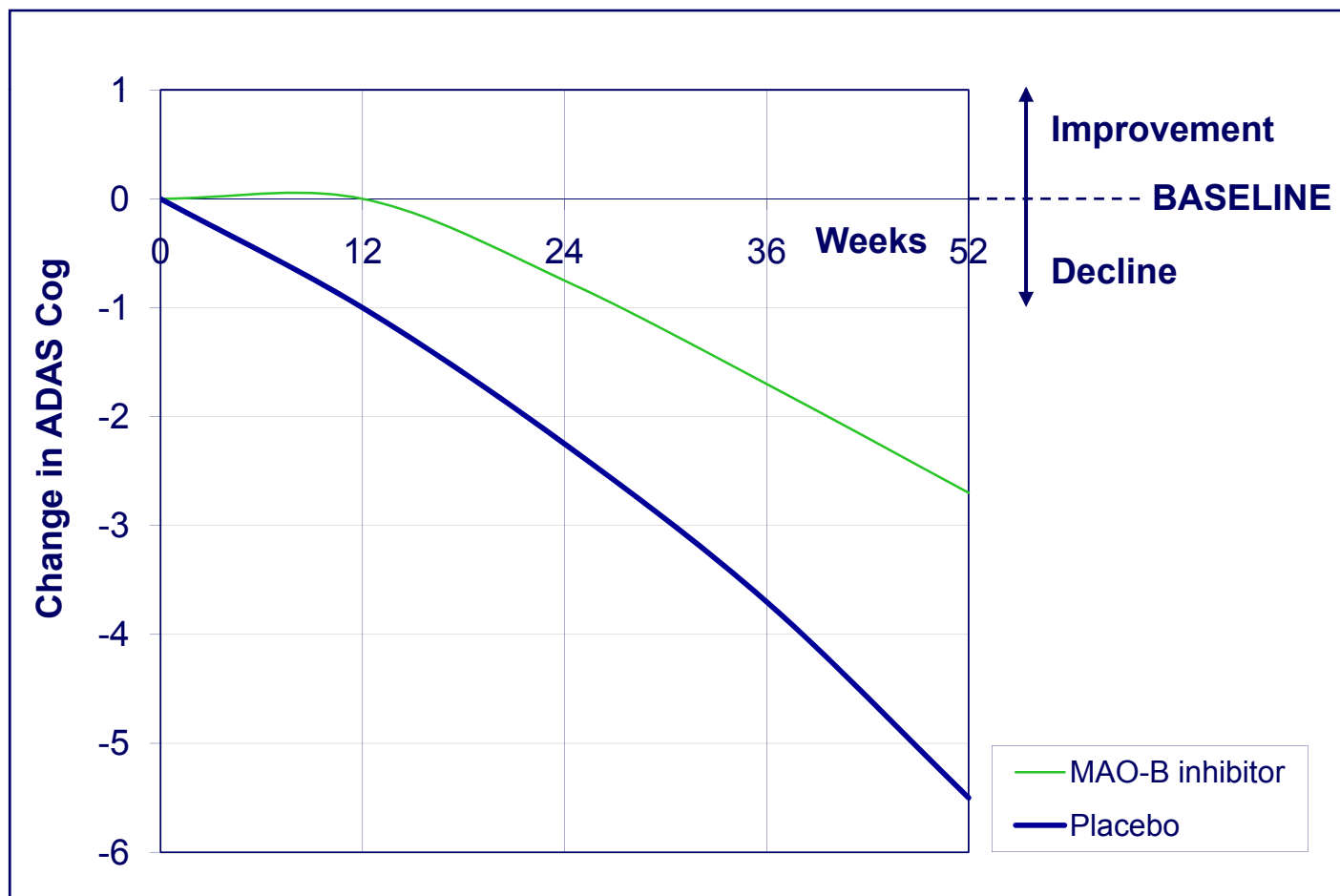
Alzheimer's Disease patient vs age-matched healthy individual

- MAO-B is normally present in the brain and is responsible for breakdown of certain neurotransmitters
- Activity of MAO-B is linked to production of reactive oxygen species, molecules that cause oxidative stress which can result in neuronal damage
- Excessive MAO-B activity in Alzheimer's Disease may contribute to neurodegeneration
- Blocking the activity of MAO-B should reduce oxidative stress and this may slow the progression of Alzheimer's Disease

# Theoretical consequence of slowing progression of symptoms in AD

Slower rate of decline on cognitive tests such as ADAS-Cog<sup>1)</sup>

- Slowing the progression of symptoms would be reflected in a slowing of the rate of decline in cognitive tests such as ADAS-Cog<sup>1)</sup>
- This would result in a progressively increasing divergence between placebo and MAO-B-inhibitor treated groups
  - No acute symptomatic effect expected



## Ideal molecule to test the mechanism of MAO-B inhibition in AD patients

---

EVT 302 Profile: Highly selective, safe, well tolerated, low dose

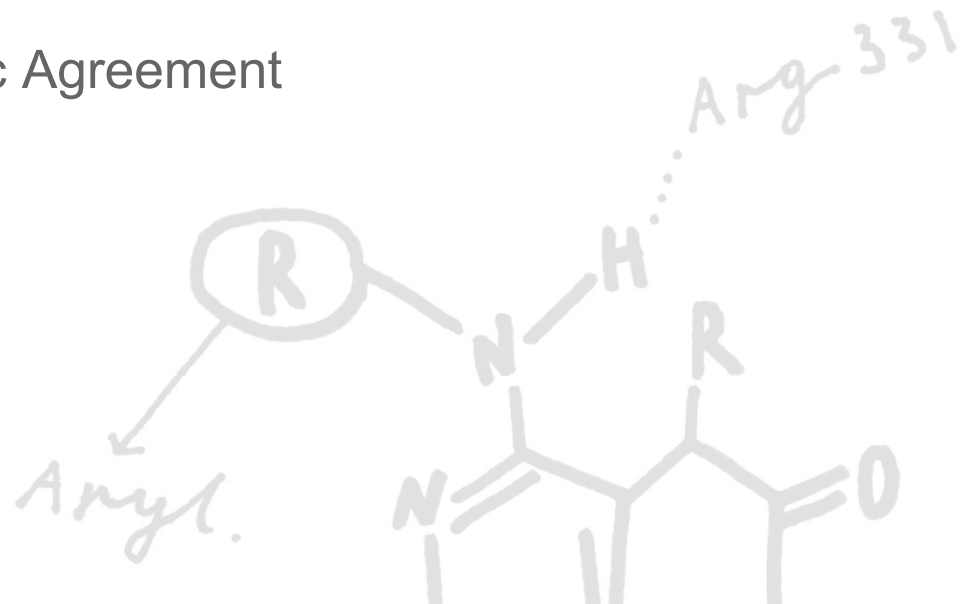
---

- Evotec has produced a robust clinical and non-clinical development package to enable Roche to move this MAO-B inhibitor programme into a large Phase II proof-of-concept trial in Alzheimer's Disease able to demonstrate a slowing of the progression of symptoms
  - Extensive Phase I package completed including single and multiple dose PET studies defining dose that provides complete MAO-B inhibition
  - Excellent safety & tolerability demonstrated (8 weeks' dosing)
- Molecule is a highly selective MAO-B inhibitor and has been demonstrated to avoid tyramine liability
  - Current MAO-B inhibitors are less selective and labelling warns of loss of selectivity at higher doses
  - Greater selectivity of EVT 302 means that no tyramine liability is observed at doses that are several multiples of the anticipated dose in Alzheimer's Disease.

## Agenda

---

- Summary and Highlights
- Market Opportunity
- MAO-B Inhibitors in Alzheimer's Diseases (AD)
- **Competitive Landscape**
- The Roche-Evotec Agreement





# MAO-B a true alternative / potential additive – all late stage programmes target $\beta$ -amyloid pathway

## Competitive Landscape in Alzheimer’s Disease Drug Development

- No agent in development has demonstrated ability to slow progression of symptoms in AD
  - All Phase III trials reported to date have failed (semagacestat, Flurizan, Alzhemed, xaliproden)
- Virtually all other approaches in late stage development for AD target the  $\beta$ -amyloid pathway and have yet to achieve clinical proof-of-concept
  - mAbs against  $\beta$ -amyloid, gamma secretase inhibitors, amyloid vaccination
  - Failure of gamma secretase inhibitors (semagacestat) has raised some questions over the  $\beta$ -amyloid hypothesis
- Evotec/Roche MAO-B programme represents an alternative and potentially complementary mechanistic approach
  - Strong scientific rationale and clinical validation, acting on a precedented target with no mechanism related safety concerns

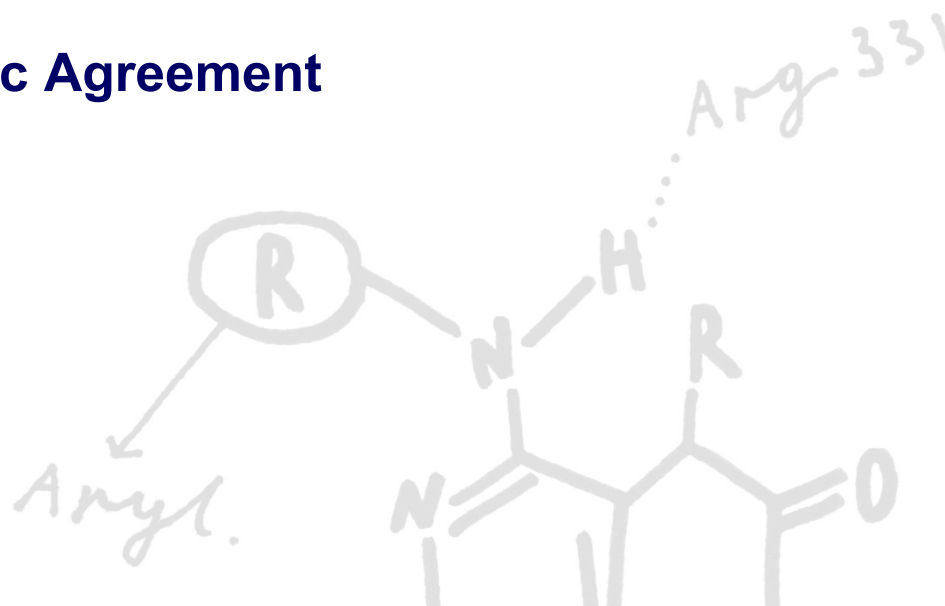
Company	Drug	Mechanism	Phase
Pfizer/J&J/ Elan	bapineuzumab	mAb against $\beta$ -amyloid	III
Lilly	solanezumab	mAb against $\beta$ -amyloid	III
Pfizer/J&J/ Elan	ACC-001	Vaccine	II
BMS	708163	Gamma secretase inhibitor	II
Roche	gantenerumab	mAb against $\beta$ -amyloid	II
Genentech/ AC Immune	crenezumab	mAb against $\beta$ -amyloid	II



## Agenda

---

- Summary and Highlights
- Market Opportunity
- MAO-B Inhibitors in Alzheimer's Diseases (AD)
- Competitive Landscape
- **The Roche-Evotec Agreement**



## A unique approach to fight AD

---

### Summary Evotec – Roche Agreement

---

- Programme represents a unique approach in Alzheimer's Disease in later stage development
- Roche are committing substantial investment into Phase IIb to achieve proof-of-concept to trigger a pivotal Phase III programme
- Proof-of-concept could be achieved very fast with potential for fast regulatory filing
- Evotec has a significant interest in the huge upside potential for the programme through development and commercial milestones and royalties
- Roche cover all development costs going forward - no risk for Evotec

# Strong news flow to come

## Outlook

### Key milestones for 2011

- |  |  |
|--|--|
| <p><b>1</b> Grow discovery alliances, build joint innovation alliances</p> | <ul style="list-style-type: none"> <li>• Build at least two significant new integrated DAB alliances (e.g. UCB) ✓</li> <li>• Deliver significant and accelerated preclinical/clinical milestones ✓</li> <li>• Show expansion success of existing alliances (e.g. ONO) ✓</li> <li>• Show operational synergies of acquisitions ✓</li> </ul> |
| <p><b>2</b> Generate optimal pipeline progress &amp; biotech values</p>    | <ul style="list-style-type: none"> <li>• Complete recruitment in 2011 for Phase II data of EVT 101 ⚡</li> <li>• At least 1 strategic deal for an early asset (P2x7 and EVT 302) ✓ <b>NEW</b></li> <li>• Generate more innovation upsides (e.g. Harvard cooperation, ...) ✓</li> </ul>  |
| <p><b>3</b> Manage innovation and path to profitability</p>                | <ul style="list-style-type: none"> <li>• Prepare growth of revenues by more than 15% y-o-y into 2012ff</li> <li>• Build profitability, without infringing innovation power</li> <li>• Keep strong strategic cash position</li> </ul>   |

**Your contact:**

Dr. Werner Lanthaler (CEO)  
Werner.Lanthaler@evotec.com

