



# INVESTOR & ANALYST PRESENTATION

*November 2013*

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# Company disclaimer

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This presentation contains forward-looking statements that provide our expectations or forecasts of future events such as new product introductions, product approvals and financial performance.

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Certain assumptions made by Lundbeck are required by Danish Securities Law for full disclosure of material corporate information. Some assumptions, including assumptions relating to sales associated with product that is prescribed for unapproved uses, are made taking into account past performances of other similar drugs for similar disease states or past performance of the same drug in other regions where the product is currently marketed. It is important to note that although physicians may, as part of their freedom to practice medicine in the US, prescribe approved drugs for any use they deem appropriate, including unapproved uses, at Lundbeck, promotion of unapproved uses is strictly prohibited.

# Strong momentum continues in Q3

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## Sales development

- Flat revenue – generic erosion on Ebixa mitigated
- New products\* up by 29%

## R&D

- US: FDA approval of Brintellix
- EU: CHMP recommendation of Brintellix and Abilify Maintena

## Financial performance

- Tight cost focus maintained
- EBIT guidance revised to DKK 1.5-1.7 billion for 2013

# Lundbeck well on track both for the year and for long-term growth opportunities



## USA

- FDA approval of Brintellix
- US products show solid performance - Onfi up 122%



## International Markets

- Azilect filed in China
- Revenue up 20% in Canada



## Japan

- In September Lexapro held a market share of 11%
- Selincro partnered with Otsuka




## Europe


- Abilify Maintena and Brintellix received positive opinion and marketing recommendation from CHMP
- Selincro filed for registration in Russia

# Very strong uptake for Treanda in Canada

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- ★ 1,500 patients treated with Treanda
- ★ YTD revenue of CAD 13.2 million
- ★ After just 2 years, Lundbeck Oncology team ranked 2nd by blood cancer KOLs

 Lundbeck Oncology  
Oncologie



**Lundbeck  
in oncology**

We believe in being open to new knowledge.  
But even more, our sense of humanity defines  
how we reach out to another human being  
and the world around us.

**Lundbeck  
en oncologie**

Nous croyons en l'ouverture d'esprit face aux  
nouvelles connaissances. En outre, ce qui nous  
définit le plus est notre sens de l'humanité et  
la façon dont nous tendons la main à ceux qui  
nous entourent.

# Abilify Maintena sales to date are in line with projections

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- ★ ...sales were USD 14.9 million in the third quarter according to IMS data<sup>1)</sup>
- ★ ...final EU approval expected before year end
- ★ ...is set to expand the long-acting market in schizophrenia



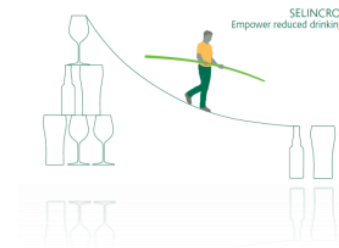
1) IMS data has a capture rate of approximately 60%



# Two positive HTA reviews on Selincro – first commercial launch in the Netherlands

- ★ ...in the quarter Selincro realized DKK ~2 million in sales
- ★ ...received first full reimbursement in the Netherlands and Scotland
- ★ ...first commercial launch in the Netherlands in October
- ★ ...partnered with Otsuka in Japan

**Selincro®**  
nalmefene 



# Continued positive progress on development projects

## Regulatory review

- ★ Brintellix approved and recommended for approval in the US and EU respectively
- ★ Abilify Maintena recommended for approval in Europe
- ★ Broader FDA approval of Sabril for adjunctive treatment option for children
- ★ IV carbamazepine to be filed in 2013

## Clinical studies

- ★ Lu AE58054 phase III programme initiated
- ★ Several studies on brexpiprazole initiated

## Data presentation

- ★ Additional Brintellix data presented at ISPOR EU et al
- ★ ACNP 2013 in December

		Phase II	Phase III	Registration app.
BRAIN DISEASES	MOOD DISORDERS	Tedatioxetine* (Lu AE58054)		Brintellix (EU, CA) (Vortioxetine)
	PSYCHOSIS		Zicronapine*	Abilify Maintena (EU)
	ALCOHOL DEPENDENCE			
	DEPRESSION/SCHIZOPHRENIA		Brexpiprazole (OPC-34712)	
	ALZHEIMER'S DISEASE		Lu AE58054	
	EPILEPSY		IV carbamazepine	
NEUROLOGY	OTHER		Desmoteplase (stroke)	



# Taking depression treatment to the next level



# Brintellix on its way with a highly differentiated label

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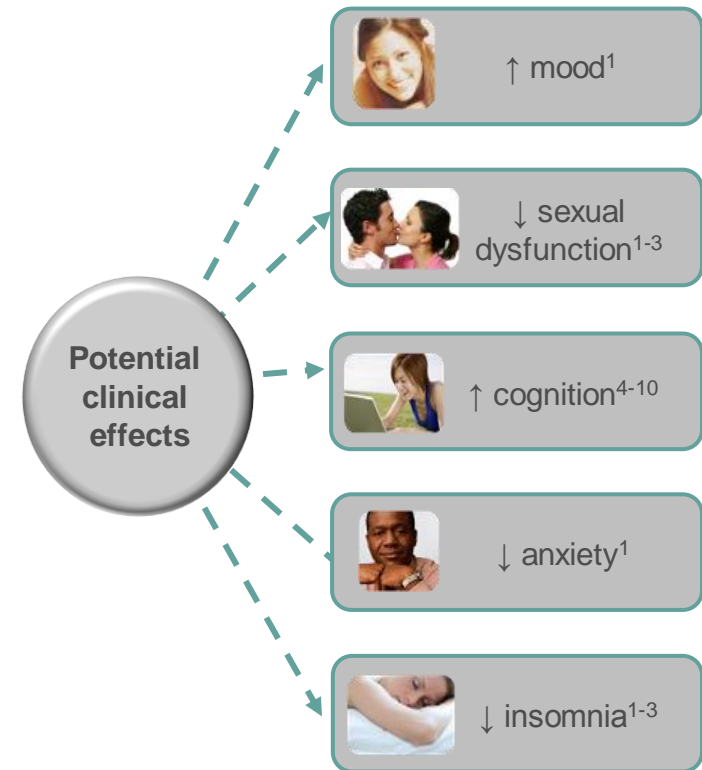
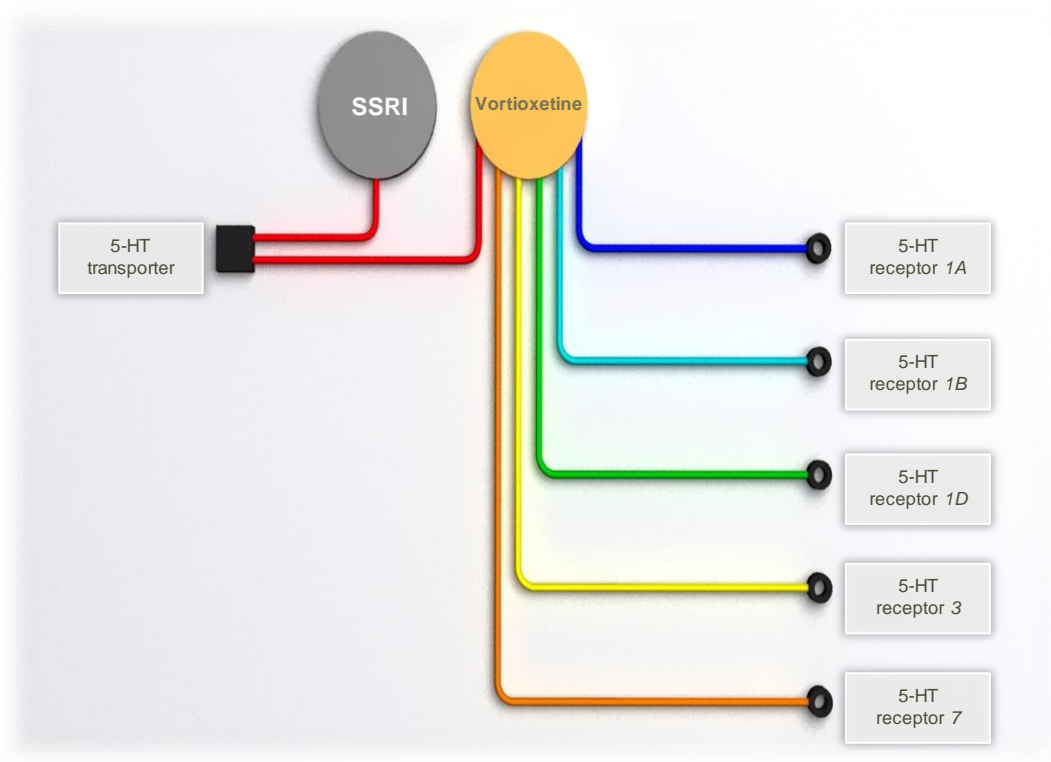
- ★ FDA approval on 30 September
- ★ Mentioning of all involved targets in MoA
- ★ Full dose range
- ★ Six positive short term studies
- ★ Flexible dosing



- ★ Positive CHMP recommendation
- ★ Mentioning of all involved targets in MoA and multimodality acknowledged
- ★ Full dose range
- ★ 9 positive short-term studies out of 12
- ★ Flexible dosing



# Brintellix: unique multimodal MoA profile that combines receptor activity and uptake inhibition



1. Mørk A et al. *Eur Neuropsychopharmacol* 2011;21(Suppl 3):S407;
2. Mørk A et al. Poster 616 presented at the Society of Biological Psychiatry 66th Annual Meeting, San Francisco, CA, USA, 12-14 May 2011;
3. Cremers T et al. Poster E004528 presented at the American Psychiatric Association 164th Annual Meeting, Honolulu, HI, USA, 14-18 May 2011;
4. Garnock-Jones KP, McCormack PL. *CNS Drugs* 2010;24:769-796

## Paving the way for Brintellix

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- ★ **Approved by FDA and recommended for approval in Europe** – regulatory process ongoing in Europe, Canada, Australia, Brazil
- ★ Over the last year we have continued to **strengthen differentiation** with supporting clinical and non-clinical data
  - *REVIVE study vs. agomelatine in patients with inadequate response to SSRI/SNRI treatment*
  - *2 ongoing cognition studies in patients with major depression*
- ★ In the **absence of a major competitor in the near future** we can invest in **building the Brintellix brand**
- ★ Opportunity to fully leverage our psychiatry presence in the **growing international markets**



# Co-development and co-commercialization agreement with Otsuka on Lu AE58054

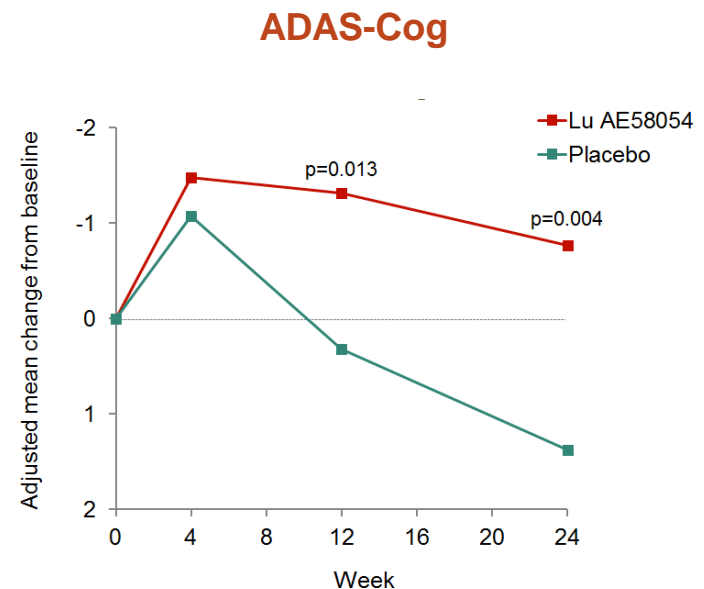
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- ★ Clinical phase II study results presented at AAIC in Boston on 16 July 2013
- ★ Lundbeck has received USD 150 million from Otsuka upon signing of agreement
- ★ Clinical phase III program in Alzheimer's initiated in October 2013
  - ★ Four trials of more than 3.000 patients
  - ★ Add-on to donepezil
  - ★ Several active dose of Lu AE58054



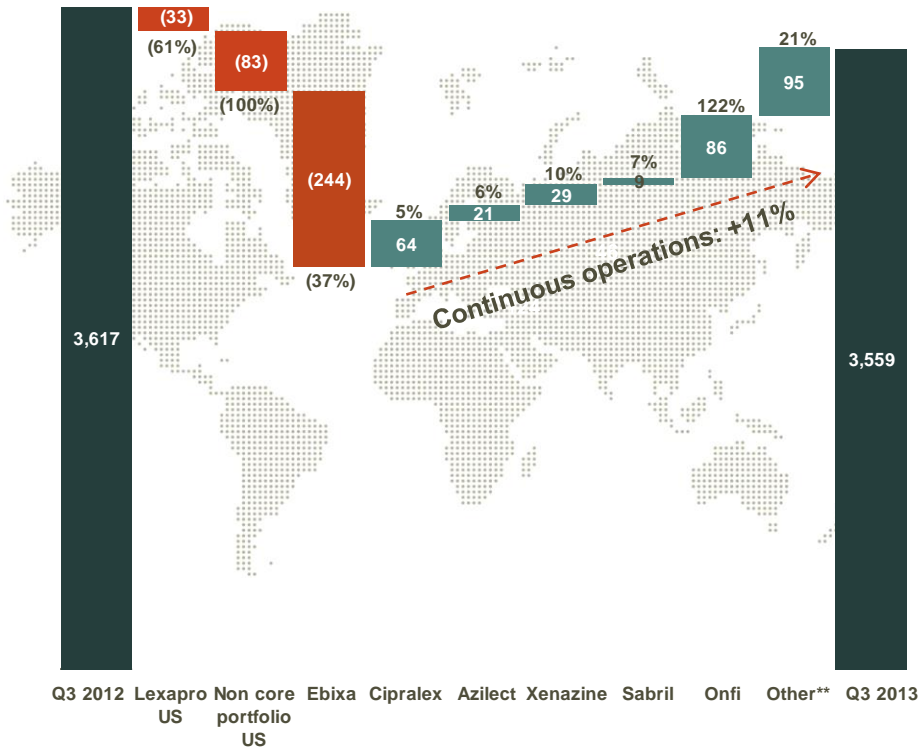
# Lu AE58054 phase II clinical results presented at AAIC in Boston

- ★ Statistically significant effect on cognitive performance with Lu AE58054 as adjunctive treatment to donepezil in patients with moderate AD (MMSE 12–19)
- ★ Trends toward improvement in measures of function (ADL) and global impression (CGIC)
- ★ Lu AE58054 appeared well tolerated in the study
- ★ ALAT or ASAT values  $>2\times$  ULN in 13 patients
  - ★ LFT abnormalities asymptomatic
  - ★ Return towards baseline values in all cases



# Continuous Operations grew 11%

## Revenue development Q3 2013 (DKK m)



- ★ Generic erosion of Ebixa mitigated by solid momentum from other products
- ★ Cipralext continues to grow in Europe and International Markets, by 4% and 6% respectively
- ★ US New Products\* showed growth of 28% in the third quarter

\*Onfi, Sabril, Xenazine and Abilify Maintena

\*\*Other includes Other pharmaceuticals, Other revenue



# Solid third quarter in 2013

DKK <b>m</b>	<b>Q3 2013</b>	<b>Q3 2012</b>	<b>Index</b>
Revenue	3,559	3,617	98
- Continuous operations*	3,002	2,697	111
R&D costs	671	684	98
- R&D%	19%	19%	
EBIT	511	661	77
- margin	14.4%	18.2%	
EPS	1.36	2.17	63
Cash flow from operations	258	541	48
Interest bearing net cash	2,787	1,340	208

\*Continuous operations = revenue excl. milestones, gains from divestment of US portfolio of non-core products, former revenue from US portfolio of non-core products , Lexapro US and Ebixa.

# Financial expectations raised for 2013

DKK	Guidance 2013	New Guidance* 2013	Expectations 2014
Revenue	14.8-15.2bn	14.8-15.2bn	~14bn
EBIT	1.3-1.7bn	1.5-1.7bn	0.5-1.0bn
(Excluding EU fine)	(1.9-2.4bn)	(2.2-2.4bn)	-
(Excluding EU fine and restructuring charge)		(2.4-2.6bn)	-

\*The new financial guidance for 2013 includes; Impairment of Sycrest product rights of DKK 210 million, DKK 284 million upfront payment related to the extension of the partnership agreement with Otsuka for Lu AE58054, USD 100 million gain related to divestment of US products, obligation and payment of the fine from the European Commission approx. DKK 700 million, the provision of DKK 200 million related to the *Fit for the future* program and USD 30 million in milestone payment related to Brintellix.

# Expected main events in 2013

## H1 2013

- Approval of Abilify Maintena in the US ✓
- Final approval of Selincro by the European Commission ✓
- Presentation of Brintellix data at APA 2013 in San Francisco, in May ✓

## H2 2013

- Presentation of Lu AE58054 data at AAIC 2013 in Boston, in July ✓
- Start of pivotal programme on Lu AE58054 in Alzheimer's ✓
- Recommendation of Abilify Maintena from CHMP in Europe ✓
- FDA approval of Brintellix in the US ✓
- Recommendation of Brintellix from CHMP in Europe ✓

# Thank you...

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# Appendix

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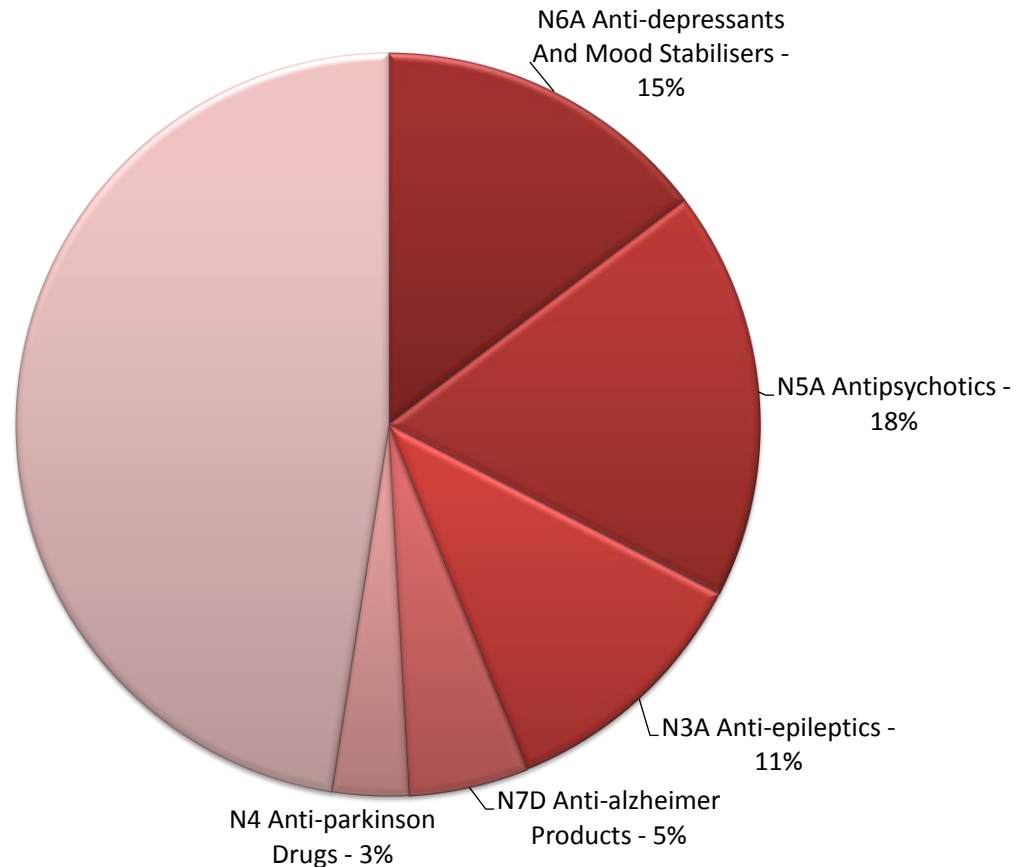
- ★ **Lundbeck overview**
- ★ Commercial operations
- ★ Pipeline
- ★ Financials
- ★ The CNS market
- ★ The Lundbeck share

# The CNS market 2012 – USD 128 billion (-5% y/y)

## The largest pharmaceutical category

### Lundbeck's current focus areas (Share of total CNS market and growth)

- ★ The CNS market represents 15% of the total pharmaceutical market
- ★ Lundbeck is also present within Huntington's disease with Xenazine...
- ★ ... and has one compound in clinical development in ischaemic stroke



# The journey started in 2009





# Our priorities are clear...

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## Execute on product launches

- Diversify product portfolio
- Ensure more balanced geographical diversification



## R&D

- Focus on research based innovation



## Drive profitability

- Use partnerships to broaden our reach
- Organisational efficiencies and high-performance culture

# ...and Lundbeck delivers on the priorities

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## Product launches

- Six products launched the last five years
- New Products increases >70% in sales in 2012
- Additional launches expected in the next 12 months

## R&D

- Selincro receives EU approval
- Abilify Maintena approved in the US and has received positive CHMP recommendation in EU
- Brintellix approved by FDA and CHMP recommended, is under regulatory process in CA and Brazil

## Profitability

- Decisions Now
- Project RECO
- Project Fit-for-the-Future

# Our vision, mission and values

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## OUR VISION

...is to become a world leader in psychiatry and neurology



## OUR MISSION

...is to improve the quality of life of people suffering from psychiatric and neurological disorders



## OUR VALUES

**Imaginative** – Dare to be different  
**Passionate** – Never give up  
**Responsible** – Do the right thing

# Lundbeck's transition

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From ...

European  
"One product"  
Company

...to the new Lundbeck



## Global growth platform

- Expand in new geographic markets



## A multiple product company

- Deliver on late-stage pipeline
- Execute new product launches
- Drive growth of diversified portfolio

# More opportunities than ever and in several therapeutic categories

Product	Peak estimate (Lundbeck sales)	Partners	Comments
Brintellix	DKK 5-10bn	Takeda	Mood disorders
Cipralex	DKK >5.5bn	-	Mood disorders
Selincro, Abilify Maintena	DKK 2-2.5bn each	- Abilify - Otsuka	Alcohol dependency, schizophrenia
Azilect, Xenazine	DKK >1.5bn each	-	Parkinson's, Huntington's
Lexapro Japan	DKK 0.8-1bn (royalty)	Mitsubishi Tanabe & Mochida	Mood disorders
Onfi, Sabril	DKK 0.5-1bn each	-	Epilepsy
Treanda, Saphris/Sycrest	DKK ~0.5bn	-	Oncology, Schizophrenia and Bipolar
Brexpiprazole	DKK >5bn	Otsuka	MDD + Schizophrenia
Lu AE58054	DKK >2.5bn	Otsuka	Alzheimer's

## Other late stage projects:

Desmoteplase (stroke), zicronapine (psychosis), tedatioxetine (MDD)

# Business development activity strengthen product offerings

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- ★ Licensing partner of choice in CNS
- ★ Strong history and experience with all forms of licensing
- ★ Using partnerships to ensure critical mass and innovation
- ★ Business development remains a priority



# Appendix

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- ★ Lundbeck overview
- ★ **Commercial operations**
- ★ Pipeline
- ★ Financials
- ★ The CNS market
- ★ The Lundbeck share



# Improving product and geographical diversification

## North America:

- + New platform for growth
- + Sabril, Xenazine and Onfi
- + Brintellix
- + Saphris (Canada)
- + Treanda (Canada)
- + Abilify Maintena
- + Brexpiprazole

## Europe:

- + Strong market position
- + Sycrest
- + Selincro
- + Brintellix
- + Abilify Maintena
- + Brexpiprazole

## Latin America:

- + Emerging markets
- + Strong commercial platform
- + Saphris
- + Cephalon brands
- + Brintellix
- + Abilify Maintena
- + Brexpiprazole

## Asia:

- + Lexapro (Japan)
- + Improved commercial platform in China
- + Saphris
- + Azilect
- + Brintellix

# China represents a major opportunity for Lundbeck

- ★ Increased presence in China
- ★ Local partnerships with Xian-Janssen and China Medical Systems (CMS)
- ★ The Chinese pharmaceutical market is fast evolving
  - ★ CNS market increased 26% in 2012
- ★ Lundbeck products has close to 25% of the depression market and Ebixa has ~30% of the Alzheimer's market
- ★ Launch of Azilect in a couple of years pending approval



## Newer products



# Xenazine – only drug approved for Huntington's chorea in the US



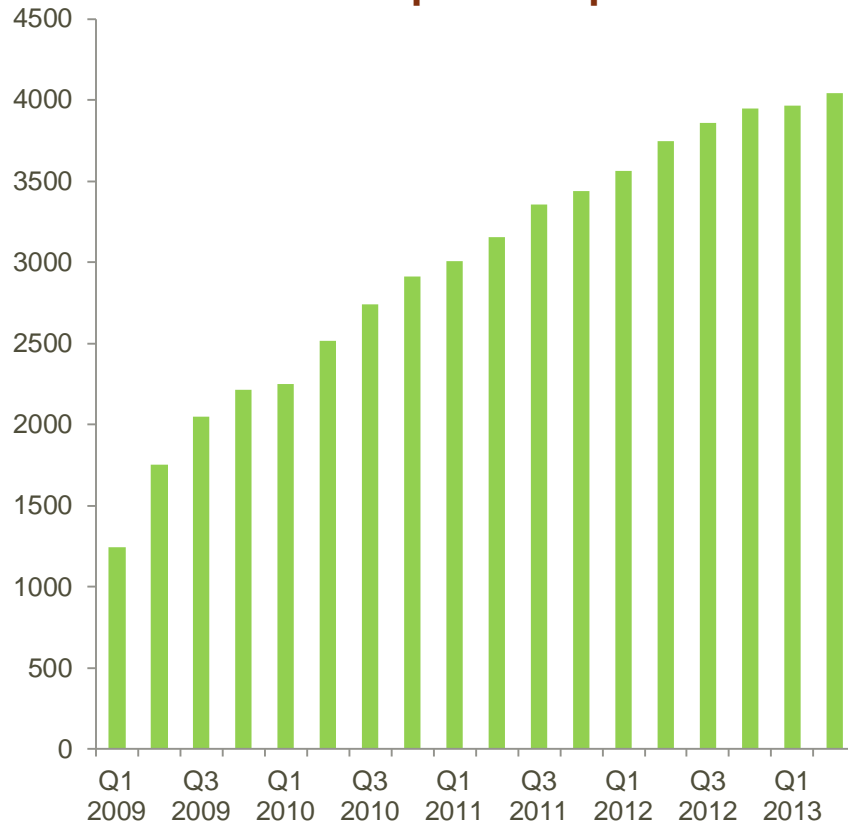
**Xenazine®**  
(tetrabenazine)  
12.5 and 25 mg Tablets

## Chorea associated with Huntington's disease (HD)

- ★ ~ 20,000 people in the US suffer from HD
    - ★ Chorea, the most common symptom of HD (~90%), is characterized by involuntary movements.
  - ★ Life expectancy is 15-20 years after onset and death often caused by pneumonia or choking
  - ★ Depression is a common co-morbid condition of the disease.
- ★ Selectively inhibiting vesicular monoamine transporter enzyme (VMAT)-2, thereby depleting pre-synaptic dopamine
  - ★ Approved for chorea associated with Huntington's disease
  - ★ Addresses high unmet medical needs and has shown strong efficacy
  - ★ Granted orphan drug exclusivity
  - ★ Data exclusivity to expire in 2015

# Xenazine patient uptake

## Xenazine patient uptake\*



\*Patients that are persistent active

- ★ Xenazine revenue for 2012 in the US was DKK 1,154 million, an increase of 41% 2011
- ★ The encouraging progress now indicates peak sales exceeding DKK 1,500 million
- ★ Xenazine continues to experience a steady uptake of patients
  - ★ At the end of Q2 2013 more than 4,000 patients were enrolled
- ★ Continued focus on helping more physicians to fully understand treatment regimen

# Sabril (vigabatrin) – addressing highly unmet needs



## Sabril

- ★ Unique method of action as a selective and irreversible inhibitor of GABA-transaminase
- ★ Aside from risk of critical vision damage (~30% of patients), Sabril is generally well tolerated
- ★ Rapid efficacy - within 2 - 3 weeks
- ★ Data exclusivity to expire in the US in 2014 (rCPS) and 2016 (IS – orphan drug status)

## Infantile spasms (IS):

- ★ ~2,500 patients/year in the US with IS
- ★ Serious disease with substantial unmet medical need
  - ★ 70-90% suffers from mental retardation, mortality of around 5%

## Refractory complex partial seizures (rCPS):

- ★ ~1 million patients in the US suffer from CPS
  - ★ 30-36% of patients are refractory
- ★ Poorly controlled by current therapies
- ★ Uncontrolled seizures has ~40x higher risk of inflicting mortality

# Onfi launch meets expectations

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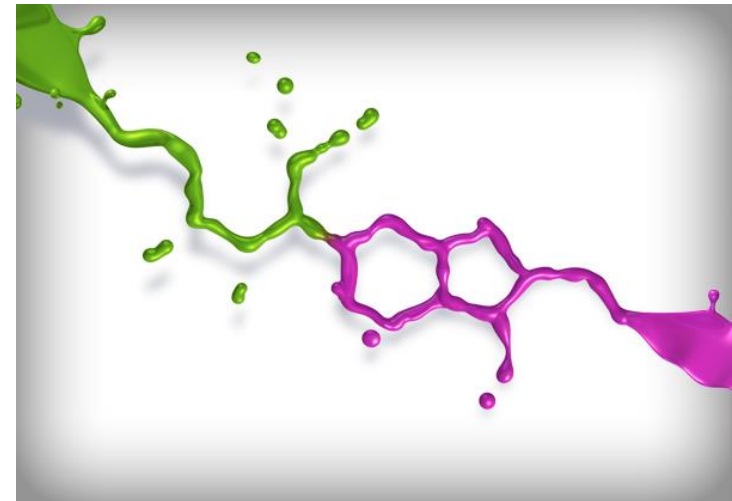
- ★ Onfi close to DKK 100 million on a quarterly basis
- ★ Launched in January 2012
- ★ Orphan drug status
- ★ Onfi approved for adjunctive treatment of seizures related to Lennox-Gastaut Syndrome (LGS)
- ★ LGS is one of the most severe forms of epilepsy and there is a clear need for new treatment options
- ★ Only 10% experience full seizure remission with current therapies
- ★ Most patients experience ongoing cognitive impairment and refractory epilepsy
- ★ Before age 11, the mortality rate is 4-7%
- ★ Around 25,000-75,000 patients





# Launch of Treanda substantially improves the growth outlook in International markets

- ★ Treanda launched in Canada indicated for two types of cancer
  - ★ Chronic lymphocytic leukaemia (CLL)
  - ★ Indolent non-Hodgkin's lymphoma (iNHL)
- ★ Lundbeck has Canadian rights to Treanda
- ★ Treanda generated revenue of USD 608 million (+127%) in 2012 in the US



[www.treanda.com](http://www.treanda.com)

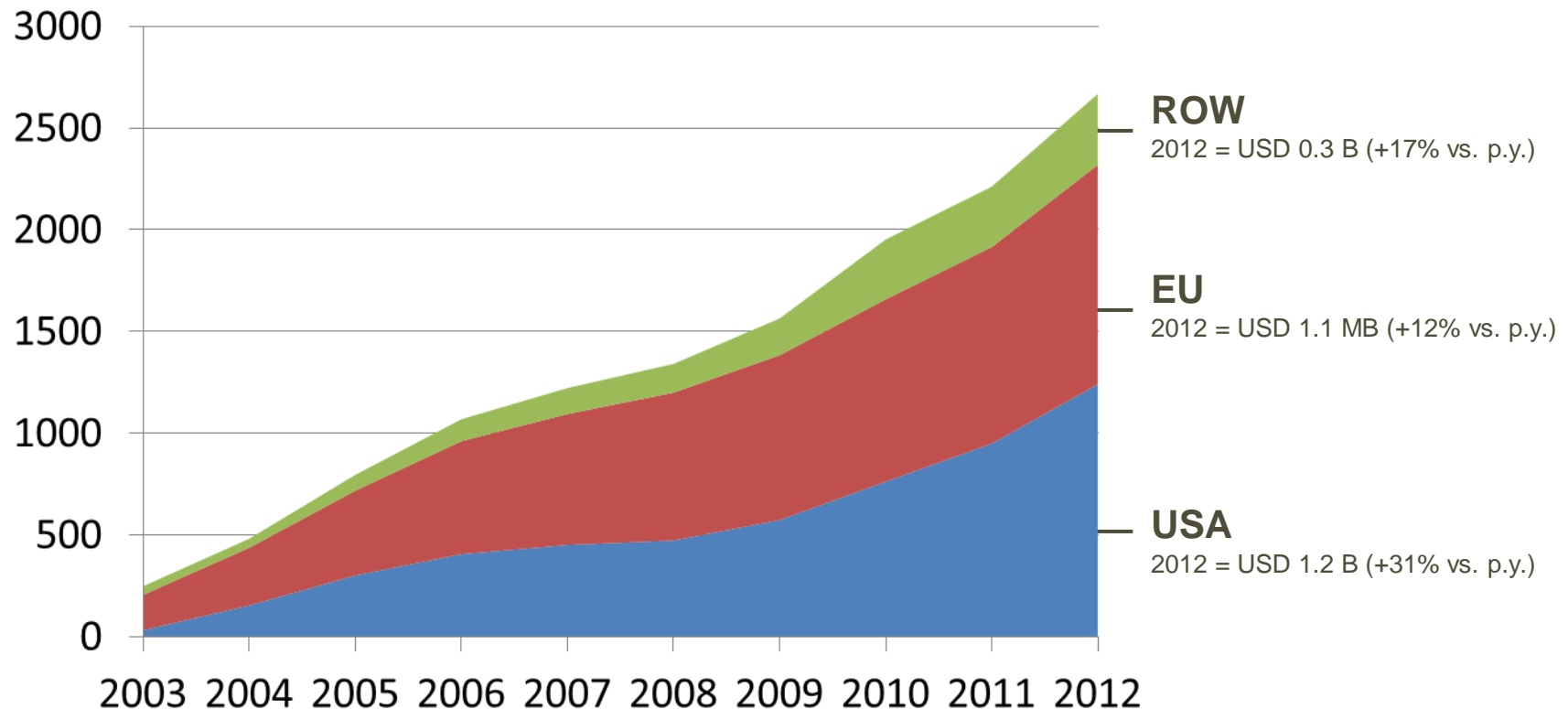
 **TREANDA**<sup>®</sup>  
(bendamustine HCl)  
for Injection  
**Built for Action**<sup>®</sup>

## Once-Monthly Abilify Maintena (aripiprazole)



# Abilify Maintena is launched into a high-growth market approaching USD 3 billion in global value

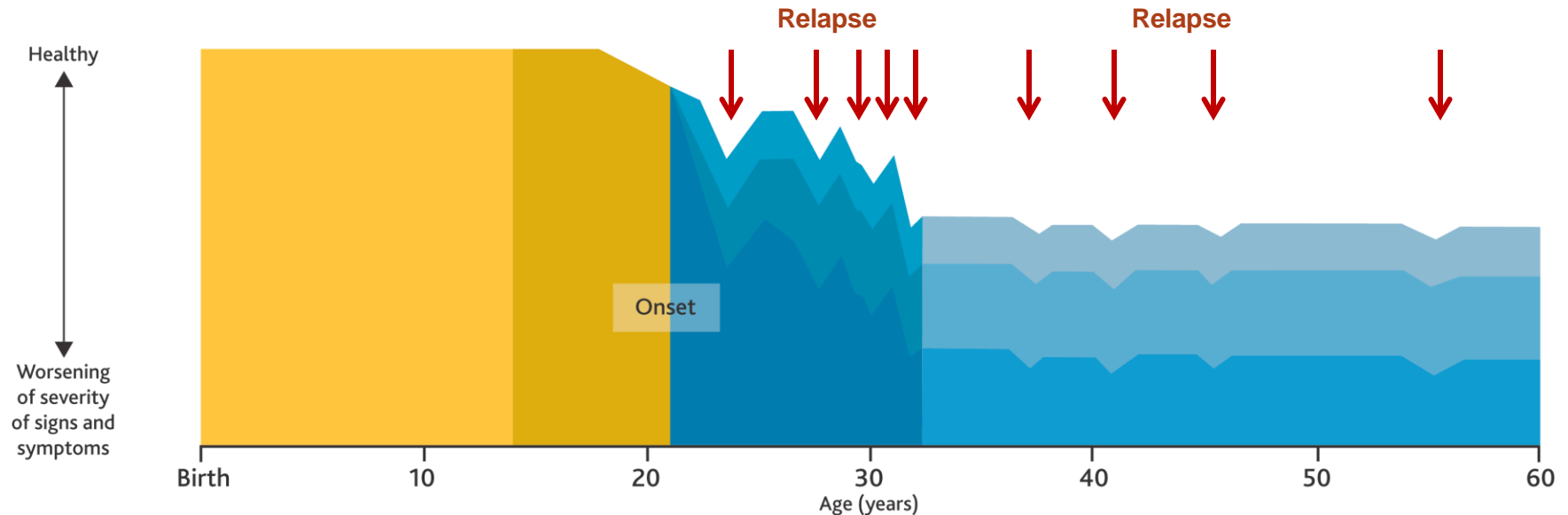
*Global market for antipsychotic long-acting injectables*  
[USD millions]



# Relapse has significant negative impact on patients with schizophrenia



## *Clinical and pathophysiological course of schizophrenia*



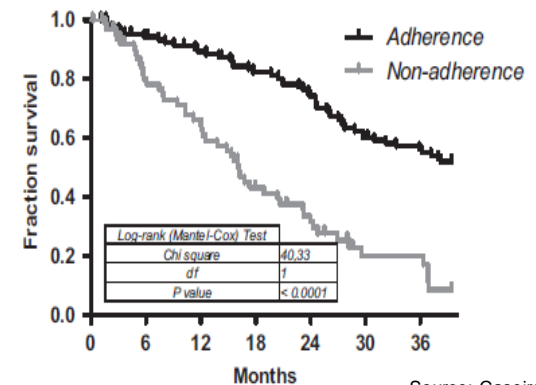
**Relapses result in functional decline and substantial, lasting neurological damage over the disease course**

# Worsening of symptoms in schizophrenia is driven by relapses



- ★ **Approximately half of patients** experience relapses and a worsening of their symptoms
- ★ This fluctuating course of the disease is devastating for a person with schizophrenia and the people around them
- ★ With each relapse, it becomes **less likely** that people with schizophrenia will return to the level of **functioning** and the life they had before their relapse

Time to relapse in adherent and non-adherent patients



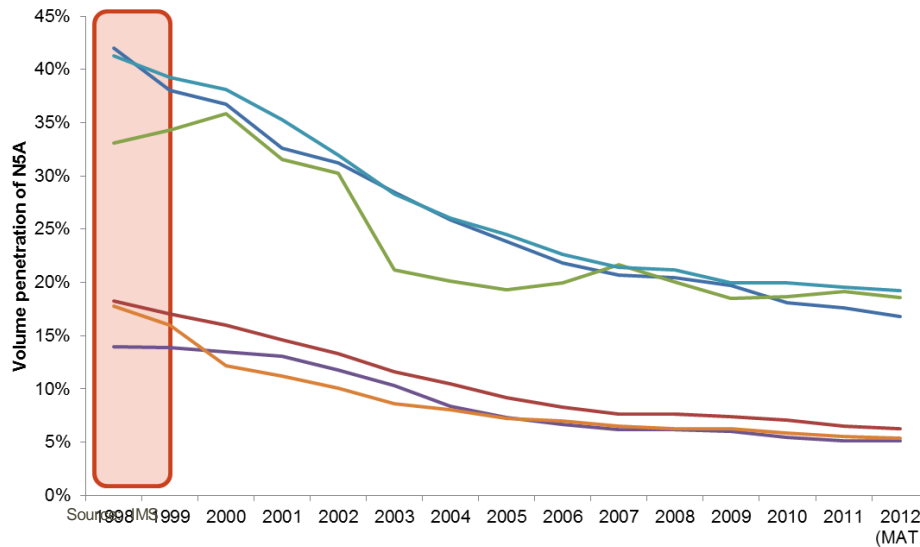
Therefore, one of the key long-term therapy goals is to **prevent relapses**



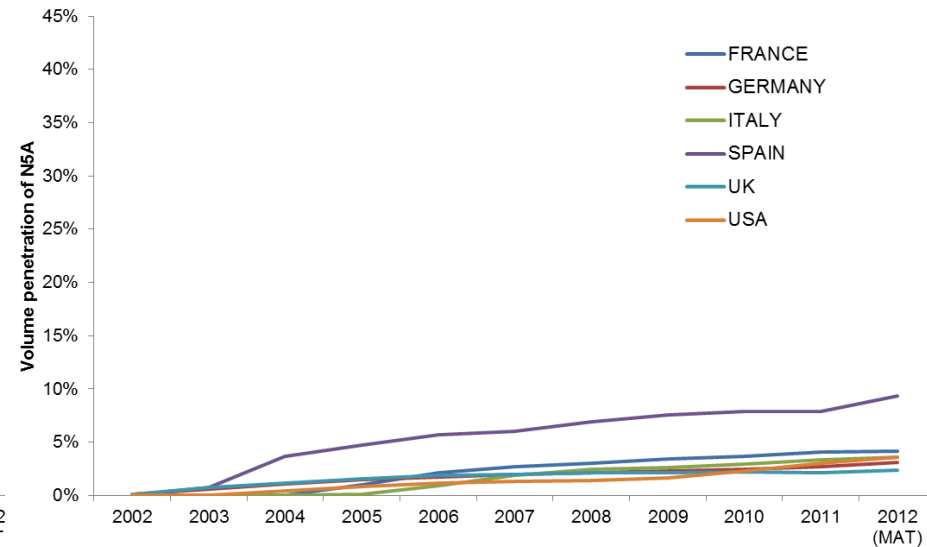
# Only 15 years ago, long-acting therapies were considered “standard of care” in several key markets



*Typical LAI penetration of N5A*



*Atypical LAI penetration of N5A*



**With only limited product options the atypical LAI market remains underdeveloped.**

LAI = long acting injectable

# Clinical programme with Abilify Maintena



Clinicaltrials.gov identifier	Estimated enrolment	Study start	Indication
NCT01663532 (phase III)	310 (US)	Oct 2012	Acute treatment of schizophrenia 12 wks. Abilify Maintena; placebo, endpoint: PANSS score
NCT01567527 (phase III)	600 (global)	Aug 2012	Maintenance treatment of bipolar I disorder 52 wks. Abilify Maintena; placebo, endpoint: relapse
NCT00705783 (phase III)*	1,025 (global)	Jul 2008	Maintenance treatment in schizophrenia (ASPIRE) 52 wks. Abilify Maintena; placebo, endpoint: relapse
NCT00731549 (phase III)	1,224 (global)	Dec 2008	Maintenance treatment in schizophrenia (ASPIRE) 52 wks. Abilify Maintena, endpoint: stability in treatment; 52 wks.
NCT00706654 (phase III)	1,148 (global)	Sep 2008	Maintenance treatment in schizophrenia (ASPIRE) 38 wks. Abilify Maintena; Abilify oral, endpoint: relapse
NCT01432444 (phase III)**	500 (US)	Sep 2011	Hospitalization rates of schizophrenic patients treated with oral antipsychotics vs. Abilify Maintena (ARRIVE US)
NCT01795547 (phase III)	286 (US)	Feb 2013	Maintenance treatment in Schizophrenia 28 wks, Randomised, Open-label Study , Abilify Maintena vs. paliperidone palmitate

\* Presented at APA 2012

\*\* Interim data presented at APA 2013

# Selincro (nalmefene)

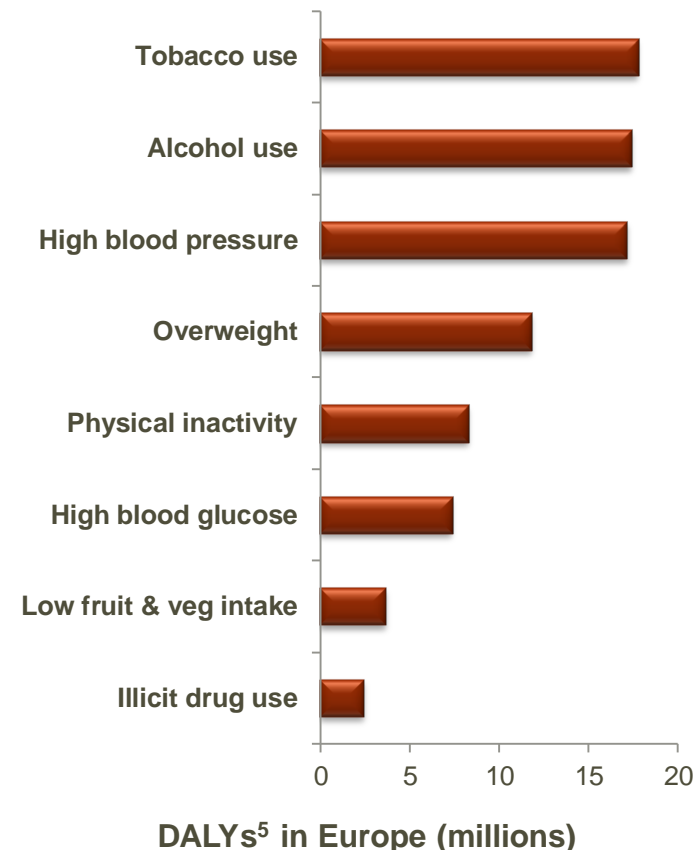
**Selincro**   
nalmefene



# Current treatment of alcohol dependence – time for a treatment paradigm shift?

- ★ The tangible costs for alcohol dependency in the EU is estimated to be EUR 125 billion<sup>1</sup>
- ★ Major-market average diagnosis rate of alcohol abuse and dependence is 17%<sup>2</sup>
- ★ Less than 10% of patients receive treatment<sup>3</sup>
- ★ Alcohol dependence remains a highly stigmatized and undertreated disease
- ★ Market is significantly under-treated and under-commercialized
- ★ Currently therapies target abstinence as the only treatment goal, which for most patients is an unacceptable goal

## Leading risk factors for burden of ill-health in Europe, 2004<sup>4</sup>



**Selincro**   
nalmefene

1) WHO – European status report on alcohol and health 2010, 2010; 2) Cognos, Addiction Disorders, 2007; 3) Alonso J et al. Acta Psychiatr Scand 2004; 109 (Suppl. 420): 47–54; 4) WHO Global Health Risk Report, 2009; 5) Disability adjusted life-years

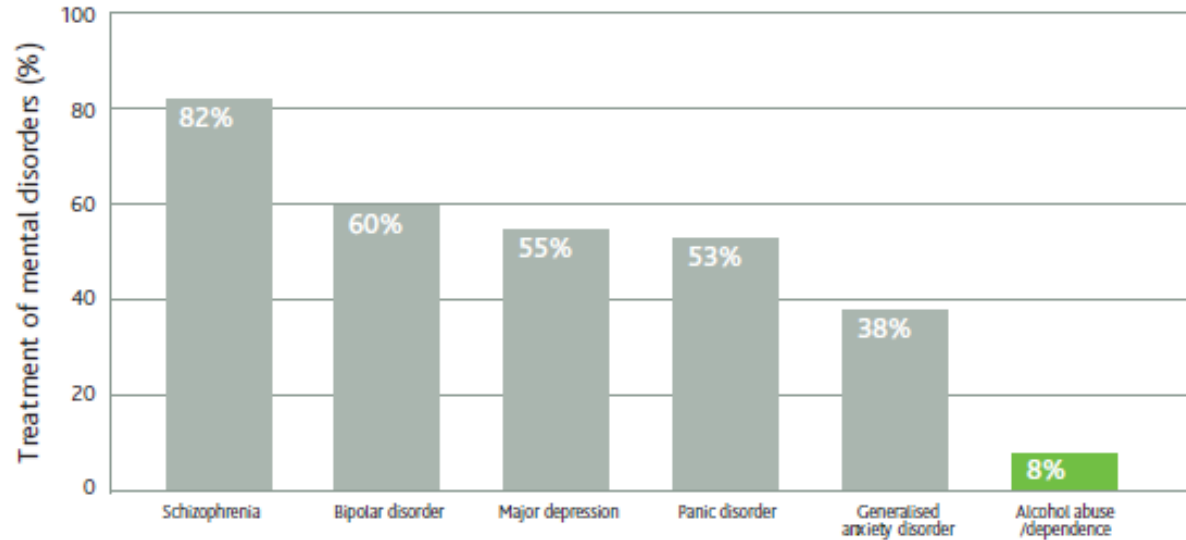
# Less than 10% of alcohol dependent patients receive treatment

**14,600,000**  
EUROPEANS ARE  
ALCOHOL DEPENDENT<sup>2</sup>



**92%**  
ARE NOT TREATED<sup>3,4</sup>

Alcohol abuse and dependence have the widest treatment gap among all mental disorders<sup>4</sup>



1. Rehm et al. Alcohol consumption, alcohol dependence, and attributable burden of disease. Centre for Addiction and Mental Health, Toronto, ON

2. Wittchen et al. Eur Neuropsychopharmacol 2011; 21(9):655–679

3. Alonso et al. Acta Psychiatr. Scand. 2004; 109: 47–54

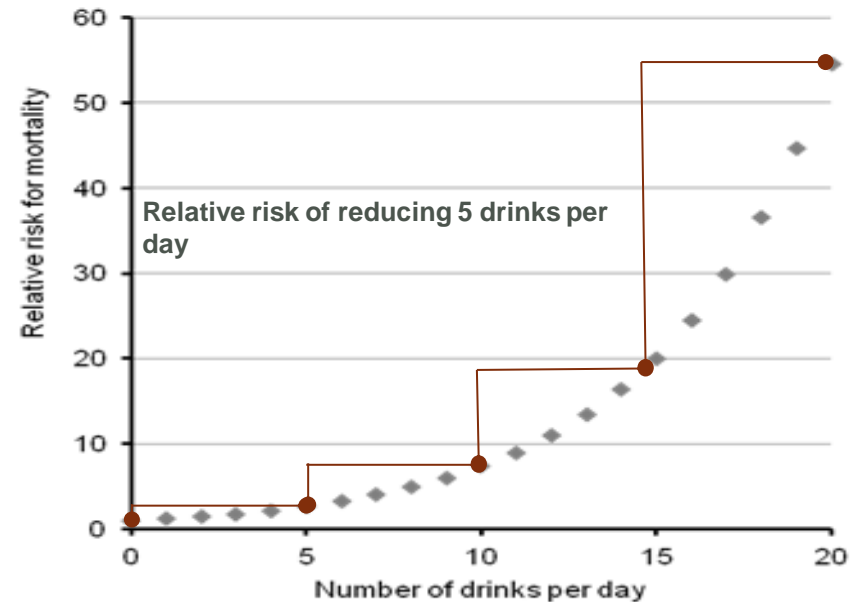
4. Kohn et al. Bull World Health Organ 2004;82:858–866

# Reducing harm by reducing high alcohol consumption



- ★ Alcohol is a causal factor in more than 60 diseases
- ★ From 10 to 4.5 drinks per day after 6 months
- ★ From 6 to 3 heavy drinking days per week
- ★ Expected to be launched in selected European countries from mid-2013

**Typical risk curve for alcohol  
(e.g., liver cirrhosis mortality)**



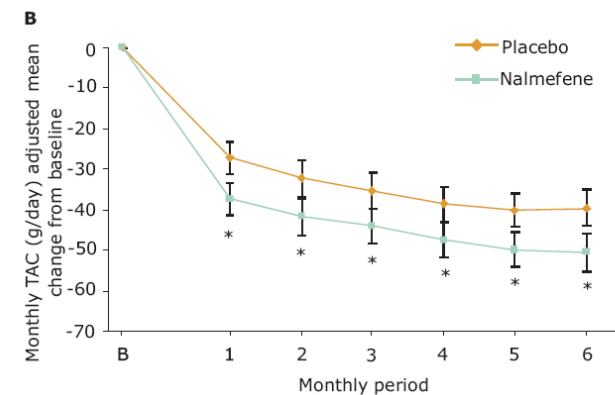
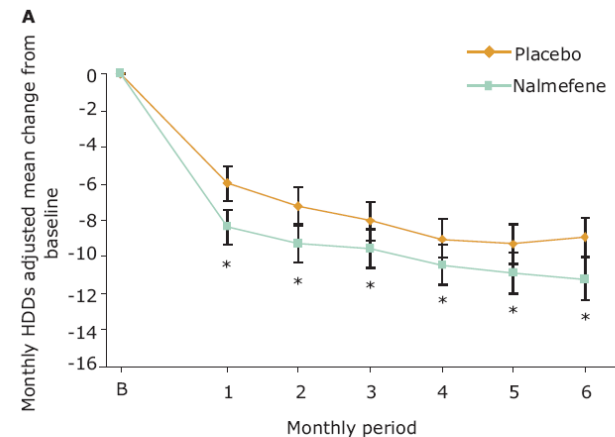
# Selincro will be the first treatment approved for the reduction of alcohol consumption

- ★ EU approval in February 2013
- ★ Selincro breaks the cycle of continuous drinking and reduced alcohol consumption by 57%



## THE SELINCRO PATIENT

- Alcohol dependent
- High drinking risk level\*\*
- No physical withdrawal symptoms/  
no need for immediate detoxification



# In clinical trials, Selincro demonstrated a significant reduction in alcohol consumption



Baseline



Equivalent to 10 bottles of wine per week

Selincro   
nalmefene

After 1 month



6 bottles

**40%**  
reduction

Selincro   
nalmefene

After 6 months



4 bottles

**60%**  
reduction

Selincro   
nalmefene

After 12 months



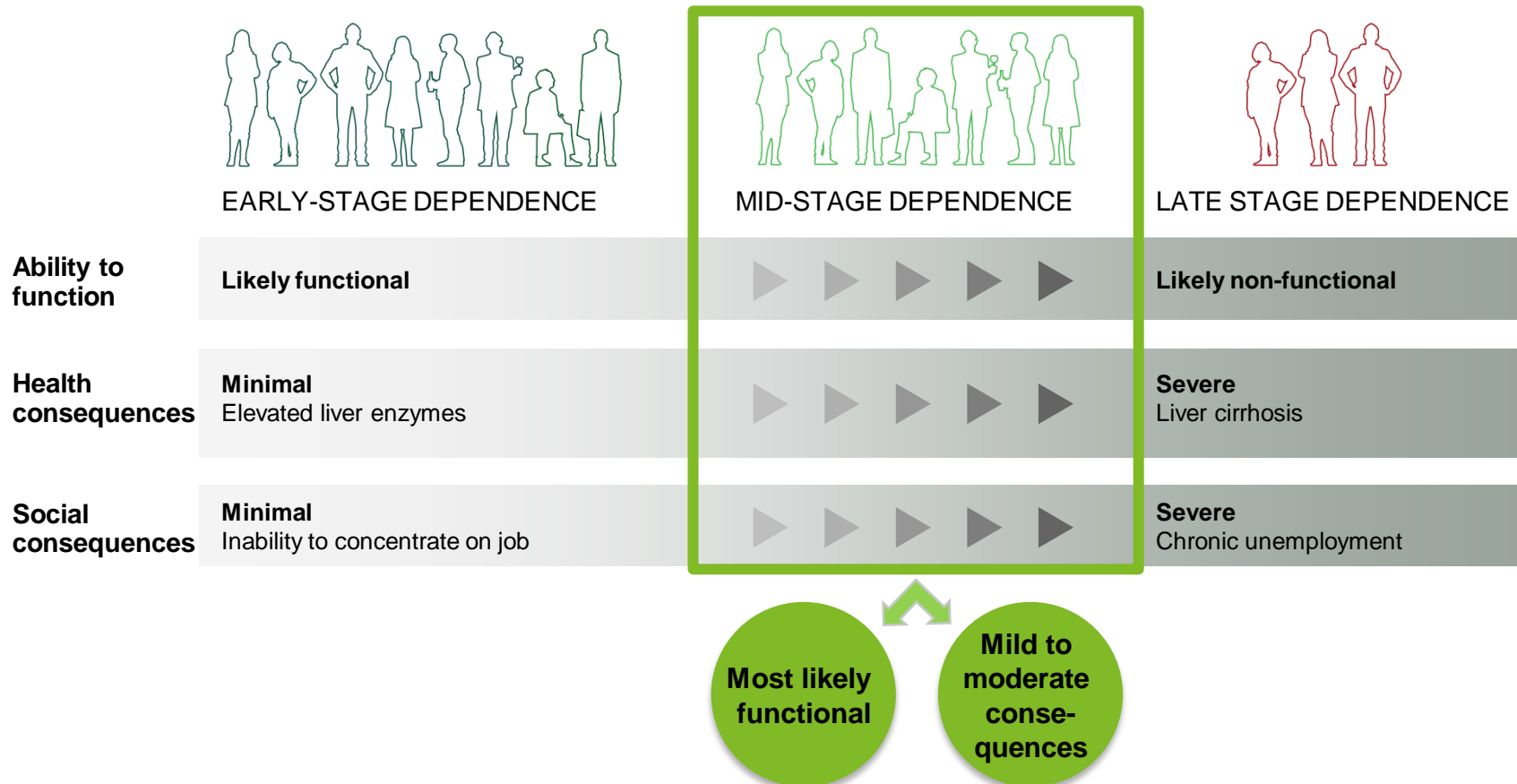
3 bottles

**67%**  
reduction

# Physicians recognize the “functional” patient with alcohol dependence as the most suitable candidate for Selincro.



## *Alcohol Dependence: A Progressive Disease*



# Selincro creates TV stories and headlines

## Example: Germany



# Appendix

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- ★ Lundbeck overview
- ★ Commercial operations
- ★ **Pipeline**
- ★ Financials
- ★ The CNS market
- ★ The Lundbeck share



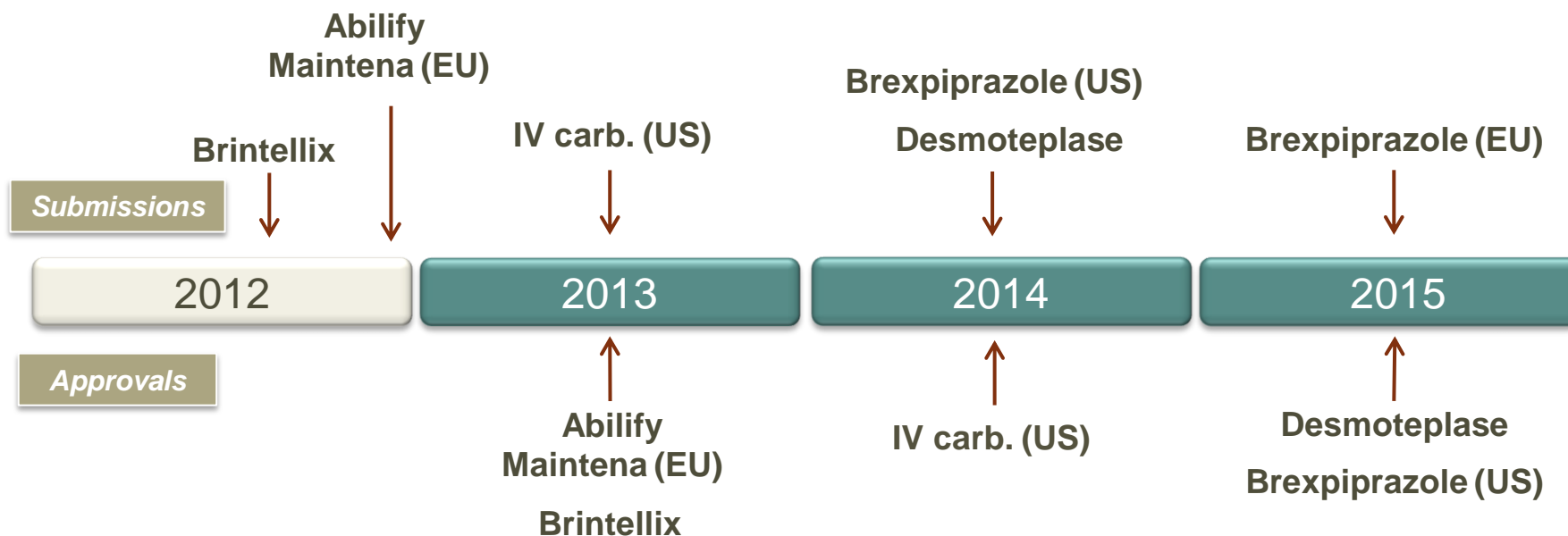
# Lundbeck invests to grow – a solid late-stage development portfolio



		Phase II	Phase III	Registration app.
BRAIN DISEASES	PSYCHIATRY	MOOD DISORDERS	Tedatioxetine* (Lu AA24530)	Brintellix (EU, CA) (Vortioxetine)
		PSYCHOSIS		Abilify Maintena (EU)
		ALCOHOL DEPENDENCE		
		DEPRESSION/SCHIZOPHRENIA	Brexipiprazole (OPC-34712)	
	NEUROLOGY	ALZHEIMER'S DISEASE	Lu AE58054	
		EPILEPSY	IV carbamazepine	
		OTHER	Desmoteplase (stroke)	

\*No active clinical programme ongoing

# Submissions and expected approvals



# Lundbeck is involved in indications costly to society and with high unmet medical needs

## DALY\* ranking (non communicable conditions)

Rank	Disease
1	Cancer diseases
2	Unipolar depressive disorder and anxiety
3	Ischaemic heart disease
4	Cerebrovascular disease
5	Chronic obstructive pulmonary disease
6	Refractive errors
7	Hearing loss, adult onset
8	Congenital anomalies
9	Alcohol use disorders
10	Diabetes mellitus
11	Cataracts
12	Schizophrenia
.....	.....
15	Bipolar disorder
.....	.....
17	Alzheimer and other dementias
...	...
23	Epilepsy
...	...
40	Parkinson's disease

\*) Disability adjusted life years, Source: Lundbeck based on Global Burden of Disease 2004, WHO

- ★ Lundbeck's focus areas rank high in terms of burden to society
- ★ These conditions are often of a serious nature and devastating for patients and family...
- ★ ... and are characterised by high unmet needs
- ★ CNS disorders are difficult to treat because of...
  - ★ the complexity of the brain
  - ★ high level of adverse effects
  - ★ the blood/brain barrier

# CNS comprises many disease areas and diseases

## Psychiatry



### Multiple sub-classifications

#### Mood Disorders

- MDD
- TRD
- Seasonal Affective Dis.
- Melancholic Depression
- Stress-related

#### Anxiety Disorders

- GAD
- Panic Disorder
- Social Anxiety
- OCD
- PTSD

#### Psychotic Disorders

- Schizophrenia
- Bipolar disorder
- Schizoaffective disorder
- Delusional disorders

#### Personality Dis.

- Paranoid PD
- Borderline PD
- Schizoid PD
- Schizotypal PD
- others

#### Addiction

- Alcohol Dependence
- Nicotine addiction
- Drug addiction
- Compulsive shopping
- Pathological gambling

#### Development Dis.

- Autism
- ADHD
- Asperger's
- Fragile-X
- Down's Syndrome

#### Eating Disorders

- Anorexia nervosa
- Bulimia nervosa
- Binge eating disorder

## Neurology



### Multiple sub-classifications

#### Movement Disorders

- Parkinson's Disease
- Huntington's Disease
- Friedreich's Ataxia
- Restless legs syndrome
- Tourette's syndrome

#### Dementias

- Alzheimer's Disease
- Vascular Dementia
- Frontotemporal Dementia
- Dementia with Lewy bodies
- Creutzfeldt-Jakob disease

#### Cerebrovascular

- Ischaemic Stroke
- Haemorrhagic Stroke
- Subarachnoid haemorrhage

#### Demyelinating Dis.

- Multiple sclerosis
- Optic neuritis
- Guillain-Barré
- Charcot-Marie-Tooth

#### Sleep disorders

- Primary insomnia
- Narcolepsy
- Sleep apnoea

#### Traumatic Injuries

- Traumatic brain injury
- Spinal cord injury

#### Pain

- Acute pain
- Migraine
- Other headaches
- Diabetic polyneuropathy
- Post-herpetic neuralgia

#### Epilepsies

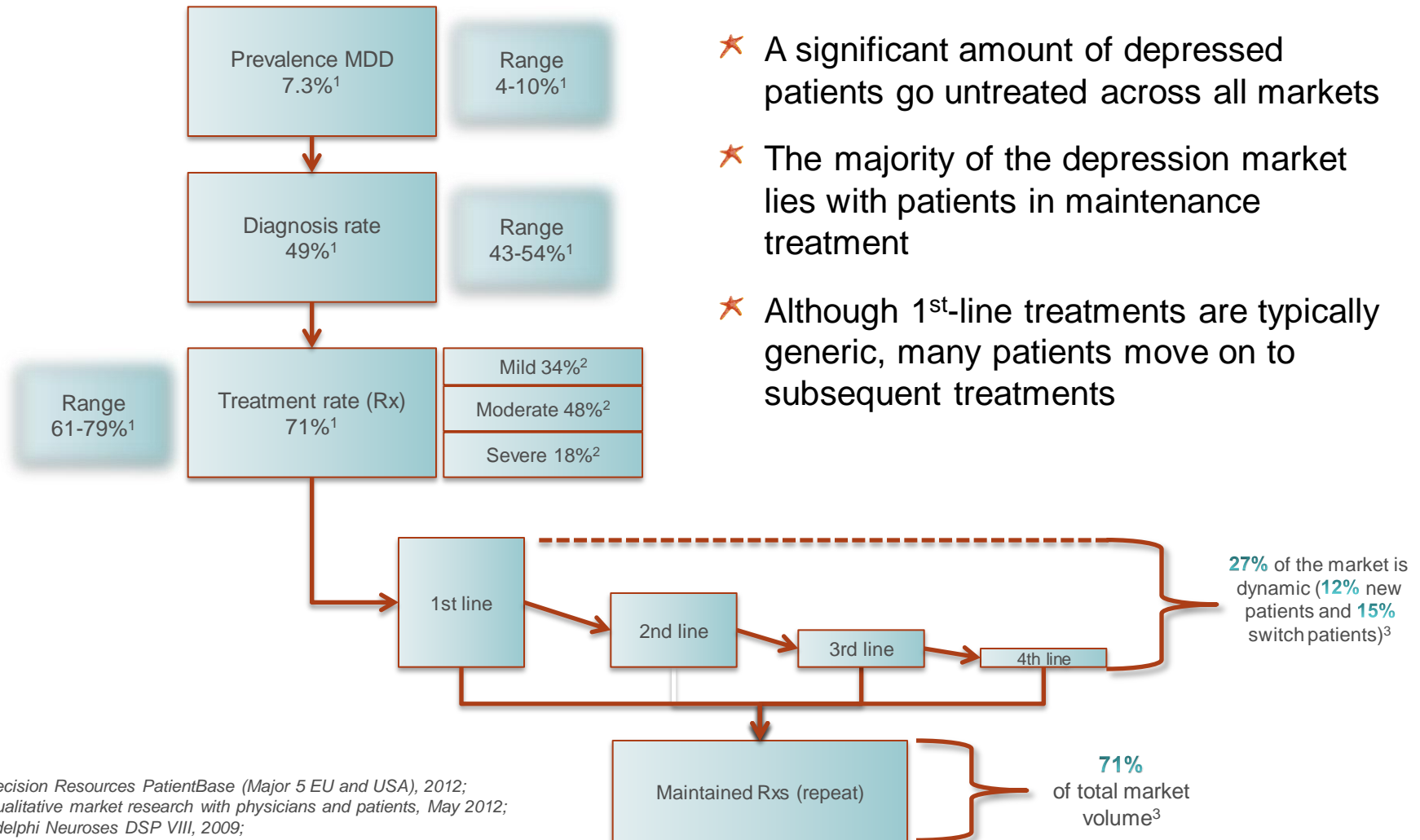
- Simple partial seizures
- Complex partial seizures
- Infantile spasms
- Lennox-Gastaut
- Temporal lobe epilepsy

 = Lundbeck presence

# Brintellix (vortioxetine, Lu AA21004)



# Depressed patient flow (merged EU and USA)



1. Decision Resources PatientBase (Major 5 EU and USA), 2012;  
 2. Qualitative market research with physicians and patients, May 2012;  
 3. Adelphi Neuroses DSP VIII, 2009;  
 4. Rush AJ et al. Am J Psychiatry 2006;163:1905-1917;  
 5. Rush AJ et al. N Engl J Med 2006;354:1231-1242

NOT FOR PROMOTIONAL USE

# Brintellix: What do we have?

*Effective antidepressant with differentiation in MoA, tolerability and cognition*



Comprehensive data package with over 7,500 individuals in studies  
70% phase III success rate vs. 48% US average for antidepressants<sup>1)</sup>

Note: Forward-looking and aspirational

1) Proportion of Failed Trials of Antidepressants in the FDA Data Sets (total). Khan A et al. J Clin Psychopharmacology 2002; 22:40-45

NOT FOR PROMOTIONAL USE

# Brintellix – thoughts on the study design



- ★ The Brintellix program was designed in line with EMA guidelines<sup>1)</sup>
- ★ Six of the 9 short-term studies included an active reference (venlafaxine or duloxetine)

## Potential consequences:

- ★ Exclusion of patients...
  - ★ If the had a history of lack of response to previous treatment with the active reference
  - ★ Known hypersensitivity to the active reference
- ★ Exclusion of non-responders and consequently inclusion of previous responders to the active reference introduces a potential bias

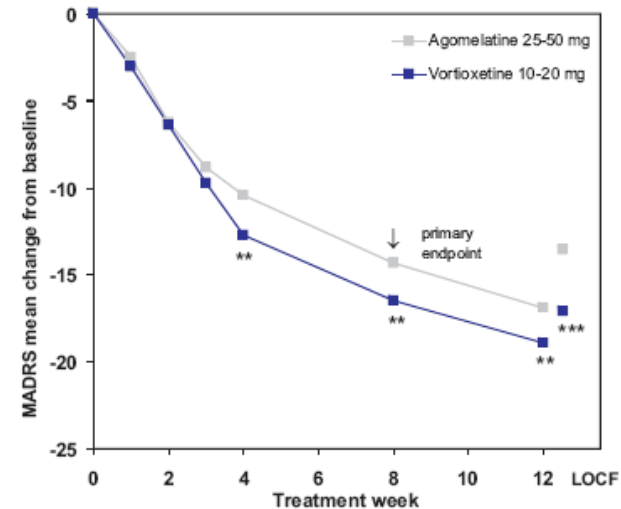
1) Note for guidance on clinical investigation of medical products in the treatment of depression



# First data from “high-dose” program on Brintellix presented at EPA in March



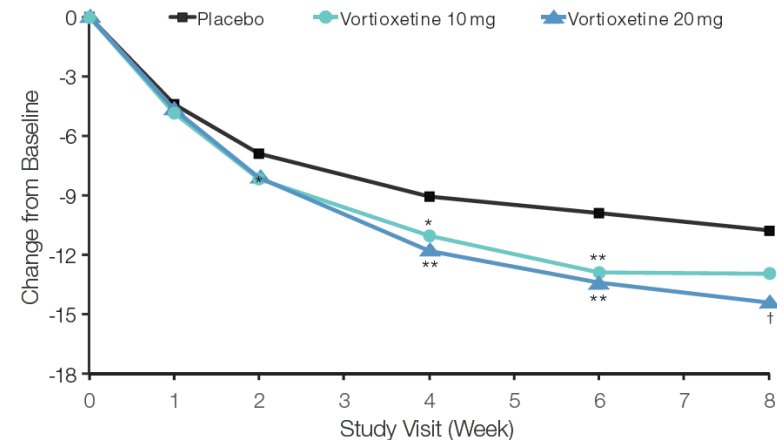
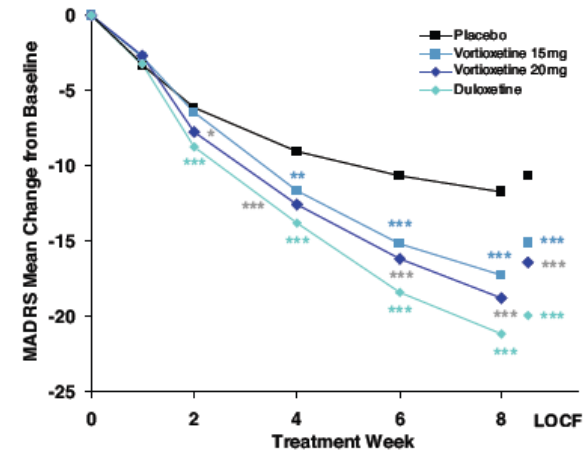
- ★ ...is a uniquely designed multimodal antidepressant that may provide unique clinical benefits
- ★ ...is significantly better versus agomelatine in patients who switched antidepressant treatment after an inadequate response to SSRI/SNRI treatment
- ★ ...showed consistent results over all endpoints
- ★ ~10 posters to be presented at APA on 18-22 May 2013



# Brintellix is a new multimodal anti-depressant with robust and broad efficacy



- ★ Efficacious in the treatment of depression in adults, elderly and when used as maintenance treatment to prevent relapse
- ★ Is efficacious in the treatment of depressive symptoms in patients with an inadequate response to SSRI/SNRI
- ★ It leads to improvement in the overall depressive syndrome, including the items of the MADRS, response and remission rates and global clinical impression as measured by the CGI-I
- ★ Improves cognitive function in depressed patients, assessed as performance on the neuropsychological tests DSST and RAVLT
- ★ Improves health-related quality-of-life outcomes (SF-36 MCS), overall health rating (EQ-5D) and overall functioning (SDS)



# Brintellix has a favorable tolerability and safety profile



- ★ Placebo-level insomnia
- ★ Low incidence of sexual dysfunction
- ★ No weight gain
- ★ No QTc prolongation, and placebo-level effects on blood pressure, heart rate and renal and hepatic assessments
- ★ In clinical studies, the incidence of nausea was low, and nausea was generally mild to moderate and transient
- ★ Brintellix treatment can be stopped abruptly without discontinuation symptoms

**Adverse Events (AEs) with an Incidence of  $\geq 5\%$  in Any Treatment Group in the 8-Week Treatment Period (APTS)**

Preferred term	Placebo	Brintellix 15mg	Brintellix 20mg	Duloxetine 60mg
Pts w. TEAEs	50.6%	57.0%	66.2%	65.3%
Nausea	10.1%	26.5%	31.8%	30.6%
Headache	7.6%	10.6%	12.6%	10.9%
Diarrhoea	3.8%	4.0%	7.3%	6.1%
Dry mouth	3.2%	3.3%	6.0%	9.5%
Dizziness	6.4%	4.6%	5.3%	10.2%
Fatigue	2.5%	4.0%	3.3%	5.4%
Hyperhidrosis	3.8%	3.3%	0.0%	7.5%

Source: J.P.Boulenger, APA2013 (Poster NR3-055)

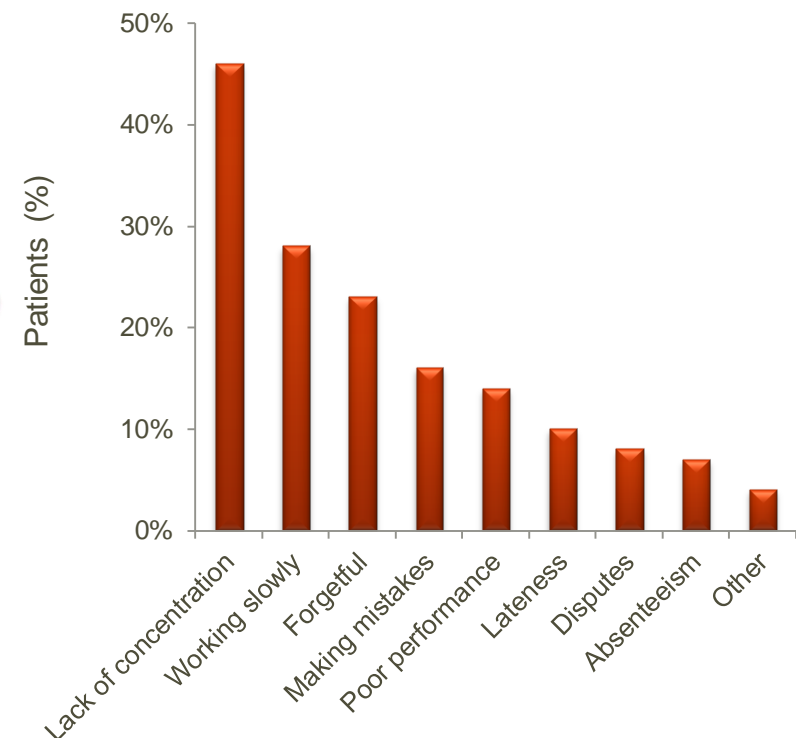
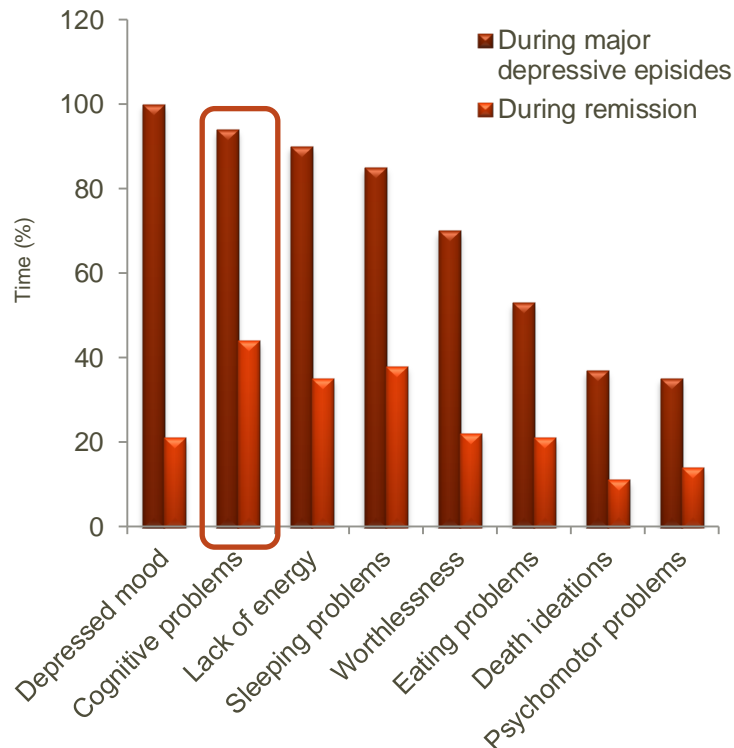
Variable	Placebo	Brintellix 15mg	Brintellix 20mg	Duloxetine 60mg
Number of subjects without sexual dysfunction at baseline				
$\Delta$ from PBO	-	-0.7%	-0.7%	17%
Number of subjects with sexual dysfunction at baseline				
$\Delta$ from PBO	-	-8.7%	6.3%	1.5%

Source: A.R. Mahableshwarkar, APA2013 (Poster NR9-01)

# Cognitive symptoms of depression are frequent and affect work productivity

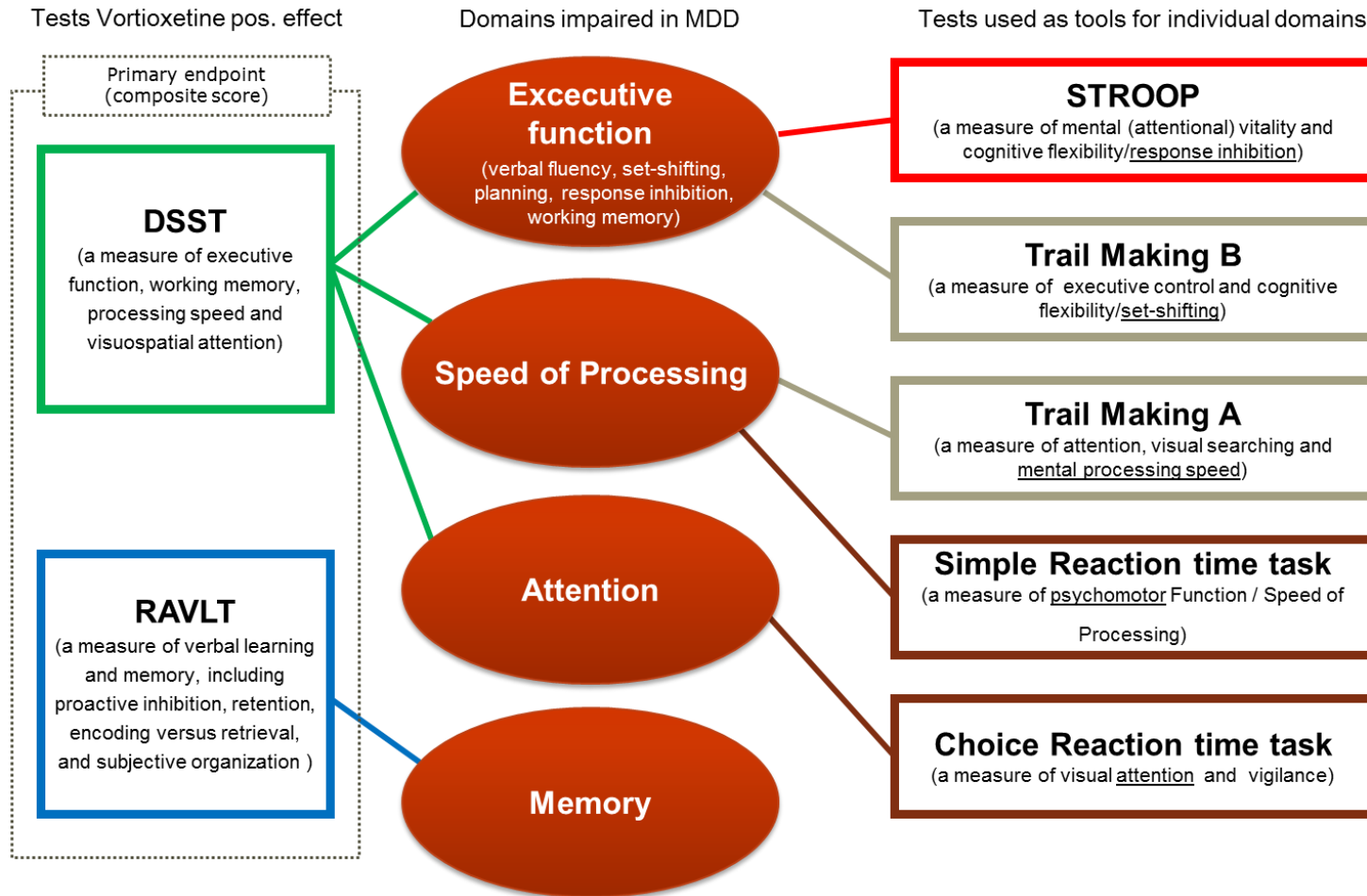
**Cognitive symptoms (difficulty concentrating, planning, decision making and forgetfulness) are very prevalent and have a direct impact at the workplace<sup>1)</sup>**

**Percentage of patients with MDD experiencing work-related cognitive dysfunction<sup>2)</sup>**



1. Conradi HJ et al. Psychol Med 2011;41:1165-1174;  
2. Adelphi Neurosis DSP VIII, 2009

# Test Selection Strategy to evaluate cognitive performance



# DSST and RAVLT were used to evaluate cognitive performance in the elderly study

## DSST<sup>3</sup>

- Measure of executive function, working memory, processing speed and visuospatial attention



*Digit Symbol Substitution Test (DSST)*

(Date of issue: 20-Aug-2008)

Reference: Wechsler D. *Wechsler Adult Intelligence Scale - third edition*. San Antonio, TX: Psychological Corporation, 1997.

1	2	3	4	5	6	7	8	9
—	⊥	⊐	└	┘	○	△	×	=

2	1	3	7	2	4	8	2	1	3	2	1	4	2	3	5	2	3	1	4

5	6	3	1	4	1	5	4	2	7	6	3	5	7	2	8	5	4	6	3

## RAVLT<sup>4,5</sup>

- Test of verbal learning, including recall and recognition



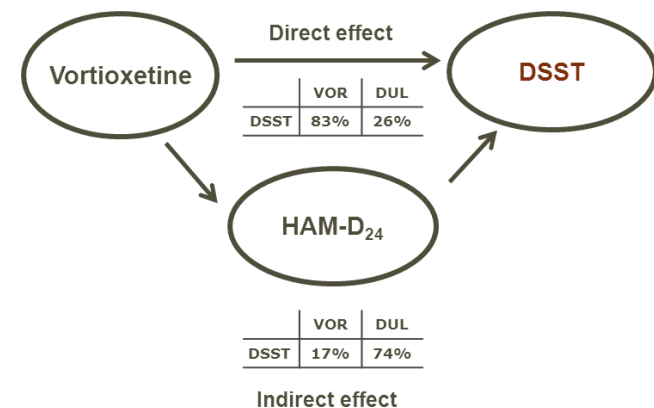
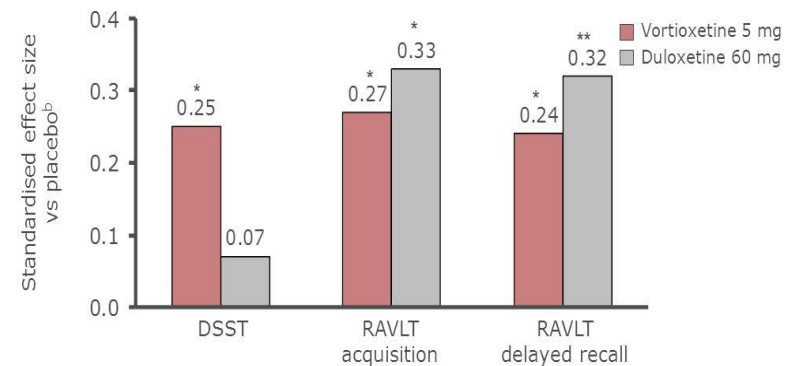
➤ Acquisition – Learning

➤ Delayed recall  
(20–30 min) – Memory

# Brintellix - cognition data in elderly patients with MDD

- ★ Significant improvement in cognitive functioning vs. placebo on DSST scale
- ★ Significant improvement in cognitive functioning vs. placebo on RAVLT scale<sup>1</sup>
- ★ Path analysis: 83% of effect on cognitive dysfunction was direct<sup>1</sup>
  - ★ Only 17% indirect effect as result of improvement in depressive symptoms
- ★ Two ongoing clinical trials in adult MDD patients with cognition tests as primary endpoints

## Brintellix' treatment effect on cognitive performance



# Brintellix: Efficacy in patients with inadequate response to SSRI/ SNRI therapy.



**John LaMattina**, Contributor  
I cover news on drugs and R&D in the pharma industry  
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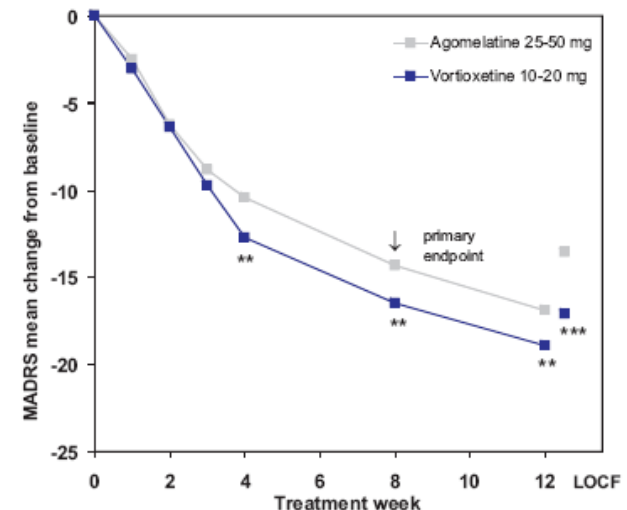
**Forbes**

PHARMA & HEALTHCARE | 4/12/2013 @ 10:18AM | 4,736 views

## New Data For Lundbeck's Antidepressant, Brintellix, Provide Insight Into Commercial Strategy

[...] What is interesting, however, is that Brintellix did help patients with MDD who had failed standard therapy. One can't help but surmise that Lundbeck will plan to develop this advantage of Brintellix in both positioning and pricing this drug. [...] This strategy differs from what would have been done 15 years ago. Back then, a company with a new antidepressant would have gotten regulatory approval for its new drug and begun marketing it against existing agents in order to compete as a first-line therapy. That strategy is no longer viable in 2013. [...] By showing that Brintellix is effective in first-line treatment failures, if it is approved, Lundbeck can have an entry into this patient population who need a treatment alternative.

Significantly better versus agomelatine in patients who switched antidepressant treatment after an inadequate response to SSRI/SNRI treatment

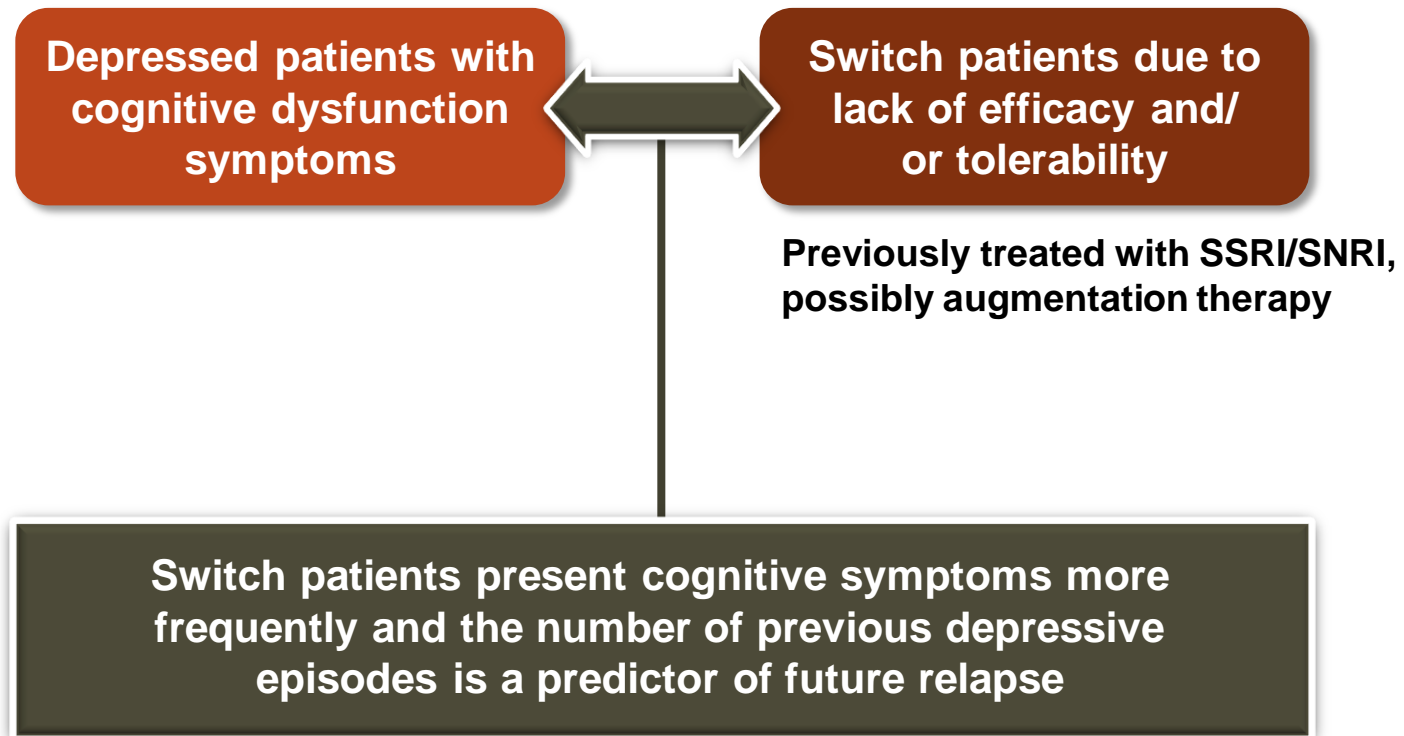


Source: xxxx



## Population groups of interest for achieving market access for Brintellix

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# Brintellix: Setting the agenda for the future treatment of major depression

Evaluating depression treatments on  
**patient relevant outcomes**

Translating clinical benefits into  
**economic value**

Restoring normal  
functioning

Impaired functioning results in  
work productivity loss

→ *Absenteeism, presenteeism*

**Indirect  
cost  
savings**

Improving the cognitive  
symptoms associated  
with depression

Residual cognitive symptoms  
increase the risk of relapse and  
recurrence

**Direct  
cost  
savings**

Addressing the  
“basics”: efficacy,  
tolerability, safety

Poor tolerability results in low  
compliance

→ *Treatment switches*

# “High dose” clinical programme using Brintellix in MDD

## Major depressive disorder

Clinicaltrials.gov identifier	Estimated enrolment	Study start	Intervention
<b>NCT01140906* #</b>	<b>600 (non-US)</b>	<b>May 2010</b>	<b>8 wks. Brintellix (15+20mg); duloxetine (60mg); Placebo</b>
NCT01255787	615 (non-US)	November 2010	8 wks. Brintellix (5+10+20mg); placebo
NCT01323478	300 (non-US)	April 2011	52 wks extension. Brintellix (15+20mg)
<b>NCT01163266* #</b>	<b>450 (US)</b>	<b>July 2010</b>	<b>8 wks. Brintellix (10+20mg); placebo</b>
<b>NCT01153009* #</b>	<b>600 (US)</b>	<b>June 2010</b>	<b>8 wks. Brintellix (15+20mg); duloxetine (60mg); placebo</b>
<b>NCT01179516 #</b>	<b>450 (US)</b>	<b>August 2010</b>	<b>8 wks. Brintellix (10+15mg); placebo</b>
NCT01152996	1,000 (US)	September 2010	52 wks extension. Brintellix (15+20mg) –by invitation only
NCT01355081	360 (Japan)	May 2011	8 wks. Brintellix (5+10mg); placebo
NCT01395147	100 (Japan)	July 2011	52 wks extension. Brintellix (5-20mg)
NCT01571453	410 (Asia)	May 2012	8 wks. Brintellix (10mg); venlafaxine XR 150mg
<b>NCT01488071 (vs. agomelatine) @</b>	<b>500 (Non-US)</b>	<b>January 2012</b>	<b>8 wks. Brintellix (10-20mg); agomelatine (25-50mg)</b>
NCT01364649 (sexual dysfunct.)	440 (US+Canada)	June 2011	Brintellix (10-20mg); escitalopram (10-20mg)
NCT01564862 (cognition)	600 (US)	April 2012	8 wks. Brintellix (10-20mg); duloxetine (30-60mg); placebo
NCT01422213 (cognition)	600 (US)	December 2011	8 wks. Brintellix (10+20mg); placebo

\* Headline conclusions communicated in May 2012. # Data presented at APA 2013 in May. @ Data presented at EPA 2013 in April 2013

# “Low dose” clinical programme using Brintellix in MDD and GAD

## Major depressive disorder

Clinicaltrials.gov identifier	Estimated enrolment	Study start	Intervention
NCT00635219 <sup>2,5</sup>	766 (non-US)	April 2009	8 wks. Brintellix (2.5+5+10mg); duloxetine (60mg); placebo
NCT00735709 <sup>2</sup>	560 (non-US)	August 2008	8 wks. Brintellix (1+5+10mg); placebo
NCT00672620	611 (US)	April 2008	8 wks. Brintellix (2.5+5 mg), duloxetine (60mg); placebo
NCT00672958 <sup>2</sup>	600 (US)	April 2008	6 wks. Brintellix (5mg); placebo
NCT00694304 (safety)	536 (non-US)	May 2008	52 wks. Brintellix (2.5-10mg flexible dose)
NCT00596817 (relapse) <sup>2</sup>	400 (non-US)	December 2007	<76 wks. Brintellix (5+10mg); placebo
NCT00707980 <sup>3</sup>	836 (non-US)	June 2008	<52 wks. Brintellix (2.5+5+10mg)
NCT00811252 (elderly) <sup>3,6</sup>	453 (US)	January 2009	8 wks. Brintellix (5mg); duloxetine (60mg); placebo
NCT00761306 (safety)	74 (non-US)	June 2007	52 wks. Brintellix (5+10mg)
NCT00839423 (phase II) <sup>1,7</sup>	429 (non-US)	August 2006	8wks. Brintellix (5+10mg); venlafaxine XL (225mg); placebo

## General anxiety disorder

Clinicaltrials.gov identifier	Estimated enrolment	Study start	Intervention
NCT00730691	781 (US)	June 2008	8 wks. Brintellix (2.5+5+10mg); duloxetine (60mg); placebo
NCT00731120	457 (US)	June 2008	8 wks. Brintellix (2.5mg+10mg); placebo
NCT00734071 <sup>4</sup>	309 (US)	June 2008	8 wks. Brintellix (5mg); placebo
NCT00744627 <sup>4</sup>	301 (Non-US)	September 2008	8 wks. Brintellix (5mg); placebo
NCT00788034 (relapse) <sup>3,6</sup>	459 (Non-US)	October 2008	8 wks. Brintellix (5mg+10mg); placebo

Publication: 1) APA 2009, 2) APA 2011, 3) APA 2012, 4) ACNP 2011, 5) European Neuropsychopharmacology (2011), 6) Int. Clinical Psychopharmacology (2011), 7) Int. Journal of Neuropsychopharmacology (2011)

# Brintellix – for EU/US registration of MDD

Short-Term (10 studies)										Long-Term
HLu 11492	HLu 11984, DF	TAK 305	HLu 13267	TAK 315	TAK 316	TAK 317	TAK 303	TAK 304	HLu 12541, Elderly	HLu 11985, Relapse prevention
6 weeks	8 weeks	8 weeks	8 weeks	8 weeks	8 weeks	8 weeks	6 weeks	8 weeks	8 weeks	OL: 12 week DB: 24-64 w
PBO 5 mg 10 mg  225 mg Venlafaxine	PBO 2.5 mg 5 mg 10 mg  60 mg Dulox.	PBO 1 mg 5 mg 10 mg	PBO  15mg 20mg  60 mg Dulox.	PBO  15mg 20mg  60 mg Dulox.	PBO 10mg 20mg	PBO 10mg 15mg	PBO 5 mg	PBO 2.5 mg 5 mg  60 mg Dulox.	PBO 5 mg  60 mg Dulox.	PBO 5 mg 10 mg
EU/Asia /CA	EU/Asia /CA	EU/ZA /Asia	EU/ZA	US	US	US	US	US	EU /CA/US	EU/CA/Asia
Positive study	Failed study, but strongly supportive	Positive study	Positive study	Positive study	Positive study	Failed or negative study	Failed or negative study	Negative study	Positive study	Positive study

# Competitors' clinical package for regulatory filing - 1

Product	Market	Indication	No. of short-term studies	No. of patients	No. of positive studies	No. of long-term studies	No. of patients	No. of positive studies
Duloxetine (Cymbalta) <i>Eli Lilly/Boehringer Ingelheim</i>	EU	MDD	6	1978	4	1	278	1
		GAD	4	1908	4	1	429	1
	US	MDD	6	1586	3	1	278	1
		GAD	3	1163	3	-	-	-
Desvenlafaxine (Pristiq) <i>Wyeth/Pfizer</i>	US (same data submitted to EMA but was decided to be withdrawn)	MDD	9	3272	4 (2 other studies nominally negative but positive on alternative analyses)	1 (but FDA decided not to review this study due to higher dose-range than proposed dosage regimen)	-	-
Agomelatine (Valdoxan) <i>Servier</i>	EU	MDD	12	4678	3	2 (one of the two studies was filed in the second submission but not in the first)	706	1 (only the study included in the second submission was positive)
Quetiapine XR (Seroquel XR) <i>AstraZeneca</i>	US	MDD (monotherapy) (only filed not approved)	5	2454	4 (only positive on primary endpoint)	1	1876	1
		MDD (adjunctive therapy)	2	939	2 (only positive in primary endpoints)	-	-	-
		GAD	4	2658	4	1	432	1

# Competitors' clinical package for regulatory filing - 2

Product	Market	Indication	No. of short-term studies	No. of patients	No. of positive studies	No. of long-term studies	No. of patients	No. of positive studies
Vilazodone (Viibryd) <i>Forest</i>	US	MDD	2	869	2	-	-	-
Mirtazapine (Remeron) <i>ScheringPlough/ Organon</i>	US	MDD	5	-	5	1	-	1
Aripiprazole (Abilify) <i>BMS/Otsuka</i>	US	MDD (adjunctive therapy)	2	743	2	-	-	-
Olanzapine/Paroxetine (Symbyax) <i>Eli Lilly</i>	US	MDD	5	1616	1	-	-	-
Bupropion SR (Wellbutrin SR) <i>GlaxoSmithKline</i>	EU	MDD	8	-	2	-	-	-
Bupropion IR (Wellbutrin IR) <i>GlaxoSmithKline</i>	EU	MDD	7	-	-	-	-	-
Bupropion XR (Wellbutrin XR) <i>GlaxoSmithKline</i>	EU	MDD	3	1564	1	1	400	1
	US	MDD	4	1401	1	-	-	-

# Competitors' clinical package for regulatory filing - 3

Product	Market	Indication	No. of short-term studies	No. of patients	No. of positive studies	No. of long-term studies	No. of patients	No. of positive studies
Sertraline (Zoloft) <i>Pfizer</i>	US	MDD	2	-	2	1	295	1
		PTSD	4	757	2	2	252 (in one of the studies – total number unknown)	2
		PD	4	686	3	1	183	1
		OCD	3	-	3	1	224	1
		OCD in children & adolescents	1	187	Study showed positive results but was found inadequate due to design for adults	-	-	-
		SAD	2	-	2	1	-	1
Levomilnacipran <i>Forest</i>	US	MDD (not yet approved)	3	>1600	3	-	-	-



# Other pipeline projects

# Brexpiprazole – a new treatment for a range of psychiatric disorders

## Brexpiprazole phase II (study no. 211)

- ★ Effective as adjunctive treatment in MDD patients with inadequate response to prior antidepressant therapy
- ★ Statistically significant reductions in MADRS total score as early as week 2 after initiation of treatment with brexpiprazole

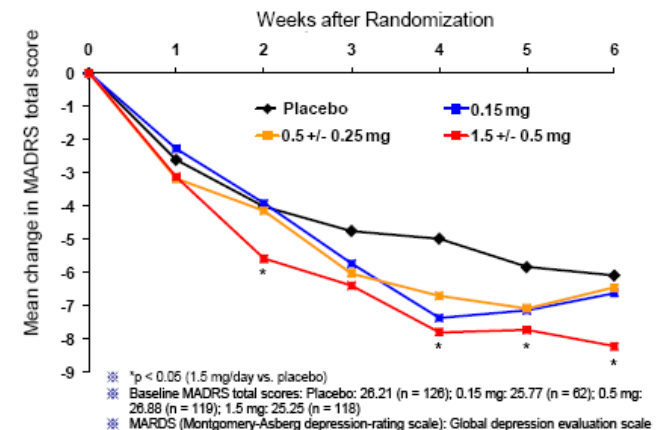
## Development status

- ★ Schizophrenia: Three phase III studies recruiting
- ★ Major depression adjunctive therapy: Five phase III studies recruiting

## Mechanism of action

- ★ Novel D<sub>2</sub>/D<sub>3</sub> receptor partial agonist
- ★ 5-HT<sub>1A</sub> partial agonist
- ★ 5-HT<sub>2A</sub> antagonist

**Phase-IIb OPC-34712 efficacy results (study no. 211):**  
**Change in MADRS total score**



# Clinical programme with brexpiprazole

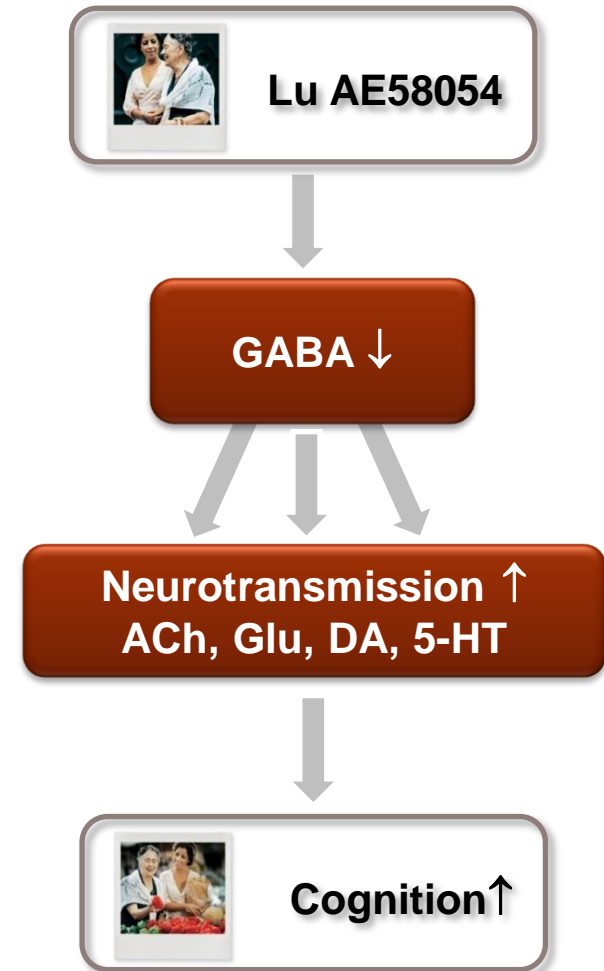
Clinicaltrials.gov identifier	Estimated enrolment	Study start	Indication
NCT01727726 (phase III)	1,340 (US)	Dec 2012	Adjunctive therapy in MDD (Delphinus) - flexible-dose. Brexpiprazole+ADT; placebo+ADT; seroquel+ADT, endpoint: MADRS score
NCT01360866 (phase III)	1,209 (US)	Oct 2011	Adjunctive therapy in MDD (Orion). 0.5-3 mg brexpiprazole+ADT, endpoint: adverse events
NCT01360645 (phase III)	925 (US)	Jul 2011	Adjunctive therapy in MDD (Pyxis). 2mg brexpiprazole+ADT; placebo+ADT, endpoint: MADRS score
NCT01360632 (phase III)	1,650 (US)	Jun 2011	Adjunctive therapy in MDD (Polaris). 1+3mg brexpiprazole+ADT; placebo+ADT, endpoint: MADRS score
NCT01838681 (phase III)	1,462 (EU)	May 2013	1-3mg. Inadequate responders in MDD; Up to 36 wks
NCT01837797 (phase III)	1,334 (elderly)	April 2013	1-3mg. Up to 20wks
NCT01810380 (phase III)	465	March 2013	To determine the efficacy and safety of brexpiprazole for the treatment of adults experiencing an acute episode of schizophrenia. Active ref: Seroquel
NCT01810783 (phase III)	140	May 2013	<4mg Safety and tolerability in schizophrenia. PANSS is secondary end-point. Up to 52 wks
NCT01668797 (phase III)	420 (US)	Oct 2012	Maintenance treatment of schizophrenia (Equator). 1-4mg brexpiprazole; placebo, endpoint: relapse
NCT01397786 (phase III)	1,000 (global)	Sep 2011	Maintenance treatment of schizophrenia (ZENITH). 1-2mg, 1-4mg brexpiprazole, Endpoint: adverse events
NCT01393613 (phase III)	660 (global)	Jul 2011	Acute schizophrenia (BEACON). brexpiprazole (low/medium/high dose), placebo, end point: PANSS score
NCT01396421 (phase III)	630 (global)	Jul 2011	Acute schizophrenia (VECTOR). brexpiprazole (low/medium/high dose), placebo, end point: PANSS score
NCT01456897 (phase III)	Na. (Japan)	Oct 2011	Long-term trial in schizophrenia.
NCT01447576 (phase II)	1,038 (US)	Sep 2009	Adjunctive therapy in MDD. 1-3mg brexpiprazole+ADT, endpoint: adverse events
NCT00797966 (phase II) <sup>1)</sup>	850 (US)	May 2009 (completed)	Adjunctive therapy in MDD. 1-4mg brexpiprazole+ADT; placebo+ADT, endpoint: depression rating scale
NCT01052077 (phase II)	773 (US)	Mar 2010 (completed)	Adjunctive therapy in MDD (STEP-D222). 1-3mg brexpiprazole+ADT; placebo+ADT, endpoint: depression rating scale
NCT01074294 (phase II)	675 (US)	Mar 2010 (completed)	Complementary treatment in ADHD. 0.25+1mg brexpiprazole+ST; placebo+ST, endpoint: efficacy/safety
NCT00905307 (phase II) <sup>2)</sup>	450 (US)	Jul 2009 (completed)	Acute schizophrenia. 4 diff. doses (0.25-6mg) of brexpiprazole (STEP 203); aripiprazole; placebo, dose establishing study
NCT01451164 (phase II/III)	N/A (Japan)	Oct 2011	Dose-finding trial in patients with schizophrenia. brexpiprazole (low/medium/high dose), placebo, end point: PANSS score
NCT0123916 (phase I)	180 (US)	Jul 2011 (completed)	Trial to Evaluate the Effects of brexpiprazole (4+12mg) on QT/QTc in Subjects With Schizophrenia or Schizoaffective Disorder
NCT01289080 (phase I)	19 (US)	Jan 2011 (completed)	Trial Evaluating 3mg brexpiprazole in Subjects With Normal Renal Function and Renally Impaired Subjects

\*ST=stimulant therapy, ADT=FDA approved antidepressant treatment

1) Published at APA 2011. 2) Published at 24th Annual US Psychiatric and Mental Health Congress, 7-11 November 2011, Las Vegas, NV, USA

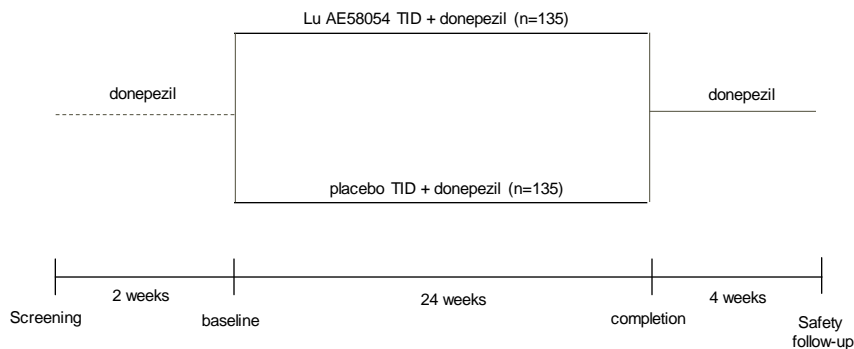
# Why could Lu AE58054 be a new valuable AD treatment?

- ★ Lu AE58054 has a different mode of action compared to existing symptomatic treatments (blockade of 5-HT<sub>6</sub> receptors)
- ★ Blocking this particular kind of serotonin receptors (5-HT<sub>6</sub> receptors) has beneficial effects on several neurotransmitter systems in the brain
- ★ Lu AE58054 has been shown to have beneficial effects on cognition in animal models
- ★ Lu AE58054 has been shown to have beneficial effects on cognition in AD patients on stable donepezil treatment



# Lu AE58054 effective in AD patients

## 24 weeks study of Lu AE58054 in combination therapy with donepezil in Alzheimer's disease



## Clinical phase II

- ★ The primary objective is to explore the effect on cognitive performance after 24 weeks of treatment
  - ★ 278 patients with moderate Alzheimer's
  - ★ Add-on to donepezil
  - ★ Treatment period of 24 weeks

## Lu AE58054 – phase II outcome

- ★ Lu AE58054 (+donepezil) demonstrated significant improvements in cognitive function compared to placebo (+donepezil), as assessed by ADAS-cog
- ★ Secondary endpoints were supportive
- ★ Lu AE58054 was considered overall to be well tolerated

# Desmoteplase – significant expansion of current treatment window in stroke

## Desmoteplase profile

- ★ Up to nine hour time treatment window
- ★ Potential to decrease bleeding complications
- ★ Potential to improve neurological outcome

## Ongoing phase III clinical studies

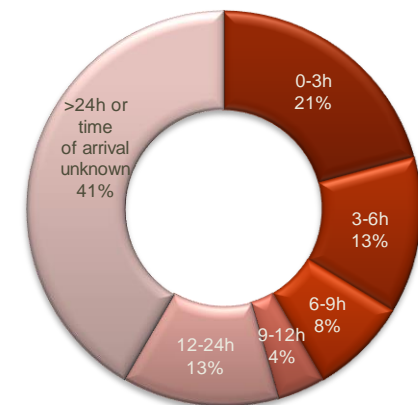
- ★ Two global phase III studies recruiting 400 and 480 patients respectively
- ★ Primary endpoint is the effect of a single dose desmoteplase (90 µg/kg) in a therapeutic window of 3-9 hours after the incidence
- ★ Filing expected in 2014

### Acute ischaemic stroke

- ★ The third most common cause of death in the industrialised world
- ★ Single most common cause of severe disability



## Arrival time among diagnosed acute ischaemic stroke patients



# Clinical phase III programme commenced with zicronapine in schizophrenia

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## Zicronapine (Lu 31-130)

- ★ Potential to treat a number of neurological and psychiatric diseases
- ★ Based on solid phase II data, a clinical phase III programme has been initiated in schizophrenia
- ★ Unique multi-receptorial profile
- ★ Affinity to monoaminergic receptors
- ★ Potent in vivo antagonistic effects at D<sub>1</sub>, D<sub>2</sub>, and 5-HT<sub>2a</sub> receptors

## Additional clinical studies

- ★ ~42 patient enrolled in a once-weekly phase II study
- ★ Study finished in 2012
- ★ ~160 patient enrolled in a phase III study
- ★ Study focused on metabolic parameters vs. risperidone
- ★ Study finished end-2012

## The clinical phase II study\*

- ★ A total of 375 patients were recruited
- ★ Zicronapine was tested at dosages between 3-10 mg/day
- ★ Clear statistically significant separation from placebo at 7 and 10mg
- ★ Convincing efficacy and safety data when compared to olanzapine

# Tedatioxetine (Lu AA24530)

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## Tedatioxetine

- ★ A multi-modal enhancer
- ★ Reuptake inhibition at monoamine transporters
- ★ Antagonist activity at 5-HT<sub>3</sub> and 5-HT<sub>2c</sub> receptors
- ★ Increases in acetylcholine, noradrenaline, dopamine and 5-HT levels in brain regions that play a key role in the regulation of mood

## Headline phase II data\*

- ★ 652 patients
- ★ Moderate to severe depression
- ★ 6 week treatment
- ★ Several doses: 5, 10 and 20 mg
- ★ Active reference: 60 mg duloxetine
- ★ Significant improvement on the primary endpoint and key secondary endpoints compared to placebo
- ★ Tedatioxetine was well-tolerated
  - ★ Drop-out rates due to serious adverse events were low in groups treated with tedatioxetine and were similar to those of duloxetine

\*Headline conclusions communicated in July 2009



# Lundbeck has significant presence in psychiatric disorders in years to come

Compound	Status	Mood disorders	Anxiety disorders	Developmental disorders	Psychotic disorders
Cipralex	Launched	Fully responsive depression			
Brintellix	Filed	Incomplete responsive dep.			
Tedatioxetine	Phase II*				
Brexiprazole	Phase III	non / inadequate responsive dep.			
Sycrest/Saphris	Launched				
Abilify Maintena	Launched (US) Filed (EU)				Maintenance treatment
Zicronapine	Phase III*				
Lu AF11167 (PDE <sup>1)</sup> )	Phase I**				

\*No active clinical programme ongoing

1) Phosphodiesterase enzyme \*\*March 2011

# Financials

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# Revenue performance Q3 2013

DKKm	Q3 2013	Q3 2012	Index	FY 2012	FY 2011	Index
Cipralex	1,464	1,399	105	5,827	5,957	98
<i>Lexapro (Japan)</i>	60	68	89	195	68	285
Ebixa	423	667	63	2,803	2,751	102
Azilect	349	328	106	1,224	1,187	103
New products*	790	611	129	2,141	1,253	171
<i>Xenazine</i>	346	317	109	1,197	852	140
<i>Sabril</i>	131	123	107	376	309	122
<i>Onfi</i>	157	71	222	255	-	-
Revenue excl. Lexapro (US)	3,538	3,563	99	14,227	13,472	106
Total revenue	3,559	3,617	98	14,802	16,007	92

\*New Products: Xenazine, Sabril, Sycrest, Lexapro (Japan), Onfi, Treanda, Selincro and Abilify Maintena

# Geographic distribution of revenue – Q3

DKKkM	Q3 2013	Q3 2012	Growth	Growth in local currency	Value market share	
					August 2013	August 2012
Europe:						
Cipralex	844	812	4%	3%	15.8%	17.0%
Ebixa	342	587	(42%)	(42%)	18.6%	26.2%
Azilect	318	305	4%	4%	15.3%	13.7%
Other Pharmaceuticals	195	187	5%	6%		
Total revenue	1,699	1,891	(10%)	(10%)		
US:						
Xenazine	342	311	10%	16%		
Sabril	131	123	7%	13%		
Onfi	157	71	122%	134%		
Other pharmaceuticals	44	142	(69%)	(71%)		
Total revenue	674	647	4%	8%		
International Markets:						
Cipralex	620	587	6%	11%	12.0%	10.8%
Ebixa	81	80	1%	1%	7.6%	8.3%
Azilect	31	23	34%	27%		
Other pharmaceuticals	234	212	10%	19%		
Total revenue	966	902	7%	12%		

Note: All market share data is from IMS Health, June 2013

# Q3 2013 – Continued satisfactory cash generation

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DKKm	Q3 2013	Q3 2012
Cash flows from operating activities	258	541
Cash flows from investing activities	(95)	15
<b>Cash flows from operating and investing activities</b>	<b>163</b>	<b>556</b>
Cash flows from financing activities	211	1
<b>Change in cash</b>	<b>374</b>	<b>557</b>
Cash	3,847	2,194
Securities	1,041	1,055
Interest-bearing debt	(2,101)	(1,909)
<b>Interest-bearing net cash and cash equivalents, end of period</b>	<b>2,787</b>	<b>1,340</b>

# Balance sheet and dividend

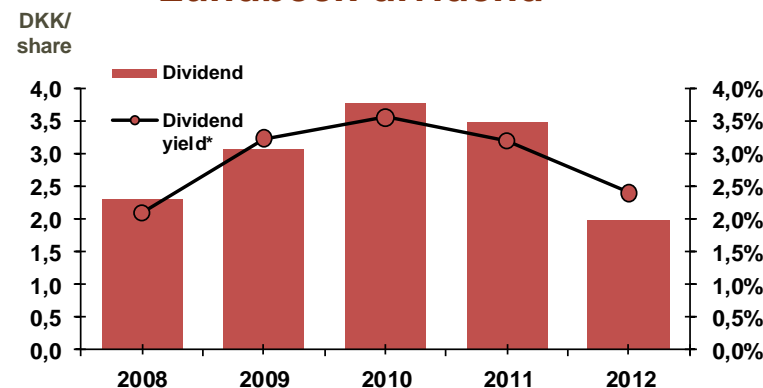
## Balance sheet

DKKm	30.09.13	30.09.12
Intangible assets	8,827	9,305
Other non-current assets	3,321	3,345
Current assets	11,298	7,811
<b>Assets</b>	<b>23,446</b>	<b>20,461</b>

Equity	13,506	13,104
Non-current liabilities	3,666	3,374
Current liabilities	6,274	3,983
<b>Equity &amp; liabilities</b>	<b>23,446</b>	<b>20,461</b>

Cash	3,847	2,194
Securities	1,041	1,055
Interest-bearing debt	(2,101)	(1,909)
<b>Interest-bearing net cash and cash equivalents</b>	<b>2,787</b>	<b>1,340</b>

## Lundbeck dividend



\* Dividend Yield = dividend per share/share price, year-end

- ★ Dividend of DKK 2.00 per share for 2012, corresponding to a payout ratio of 35%
- ★ A total of DKK 392 million and a yield of 2.4%\*\*
- ★ In 2013-2014 the pay-out ratio is expected to be 35%

\*\*based on the share price of DKK 82.9

# Revenue, yearly figures

	Revenue, DKKm					Growth, Y/Y, %			
	2012	2011	2010	2009	2008	2012	2011	2010	2009
Total revenue	14,802	16,007	14,765	13,747	11,572	(8%)	8%	7%	19%
Cipralex	5,827	5,957	5,808	5,320	4,829	(2%)	3%	9%	10%
Lexapro	575	2,535	2,443	2,451	2,464	(77%)	4%	-	(1%)
Ebixa	2,803	2,751	2,403	2,162	1,878	2%	14%	11%	15%
Azilect	1,224	1,187	1,028	769	553	3%	15%	34%	39%
Xenazine	1,197	852	610	298	-	40%	40%	105%	-
Sabril	376	309	179	-	-	22%	73%	-	-
Other pharmaceuticals	2,174	2,027	2,036	2,469	1,653	7%	-	(18%)	50%
Other revenue	626	389	258	278	195	61%	51%	(7%)	42%

# Costs, yearly figures

	DKKm					Growth, Y/Y, %			
	2012	2011	2010	2009	2008	2012	2011	2010	2009
Revenue	14,802	16,007	14,765	13,747	11,572	(8%)	8%	7%	19%
Cost of sales	3,325	3,166	2,958	2,655	2,127	5%	7%	11%	25%
Sales and distribution costs	5,274	4,526	3,952	3,608	2,799	17%	15%	10%	29%
Administrative exp.	1,641	1,602	1,453	1,430	1,302	2%	10%	2%	10%
R&D	2,915	3,320	3,045	3,196	2,990	(12%)	9%	(5%)	7%
EBIT	1,647	3,393	3,357	2,858	2,354	(51%)	1%	17%	21%
Costs, % of revenue	89%	79%	77%	79%	80%				
Cost of sales	22%	20%	20%	19%	19%				
Sales and distribution costs	36%	28%	26%	26%	24%				
Administrative exp.	11%	10%	10%	11%	11%				
R&D	20%	21%	21%	23%	26%				



# Financial terms and territory structure of the Otsuka alliance

## Milestones payments

Payment to:



- ★ Co-development and co-commercialization agreements with Otsuka

- ★ Potential peak sales (for the alliance):

- ★ USD >1bn for Abilify Maintena
- ★ USD >2.5bn for brexpiprazole
- ★ USD >1bn for Lu AE58054

- ★ Patent expiration: Abilify Maintena (2024), brexpiprazole (>2025), Lu AE58054 (>2030)

- ★ Selincro in Japan recently added to the alliance

	Abilify Maintena	Brexpiprazole	Lu AE58054	Selincro
Development milestones/upfront	USD 200m	USD 600m <sup>2)</sup>	USD 150m	EUR 105m*
Approval milestones	USD 275m <sup>1)</sup>	USD 300m <sup>2)</sup>	USD 300m	Un-disclosed
Sales milestones	Up to USD 425m depending on sales development		Up to USD 375m depending	Un-disclosed

1) USD 100m upon US approval, USD 75m upon EU approval in schizophrenia, and USD 50m US and EU for a second indication. 2) USD 100m (US) and USD 50m (EU) for each of the two first indications  
2) Development milestones of up to USD 600m after which shared development costs between parties

## Lundbeck's share of revenue and costs

	Abilify Maintena	Brexpiprazole	Lu AE58054	Selincro
USA	20%	45%	55%	-
EU-5, Nordic and Canada	50%	50%	50%	-
Other Lundbeck territories	65%**	65%**	~50%***	Un-disclosed

\* Includes sales milestones

\*\* All regions except Asia, Turkey and Egypt

\*\*\* All regions except Thailand and Vietnam

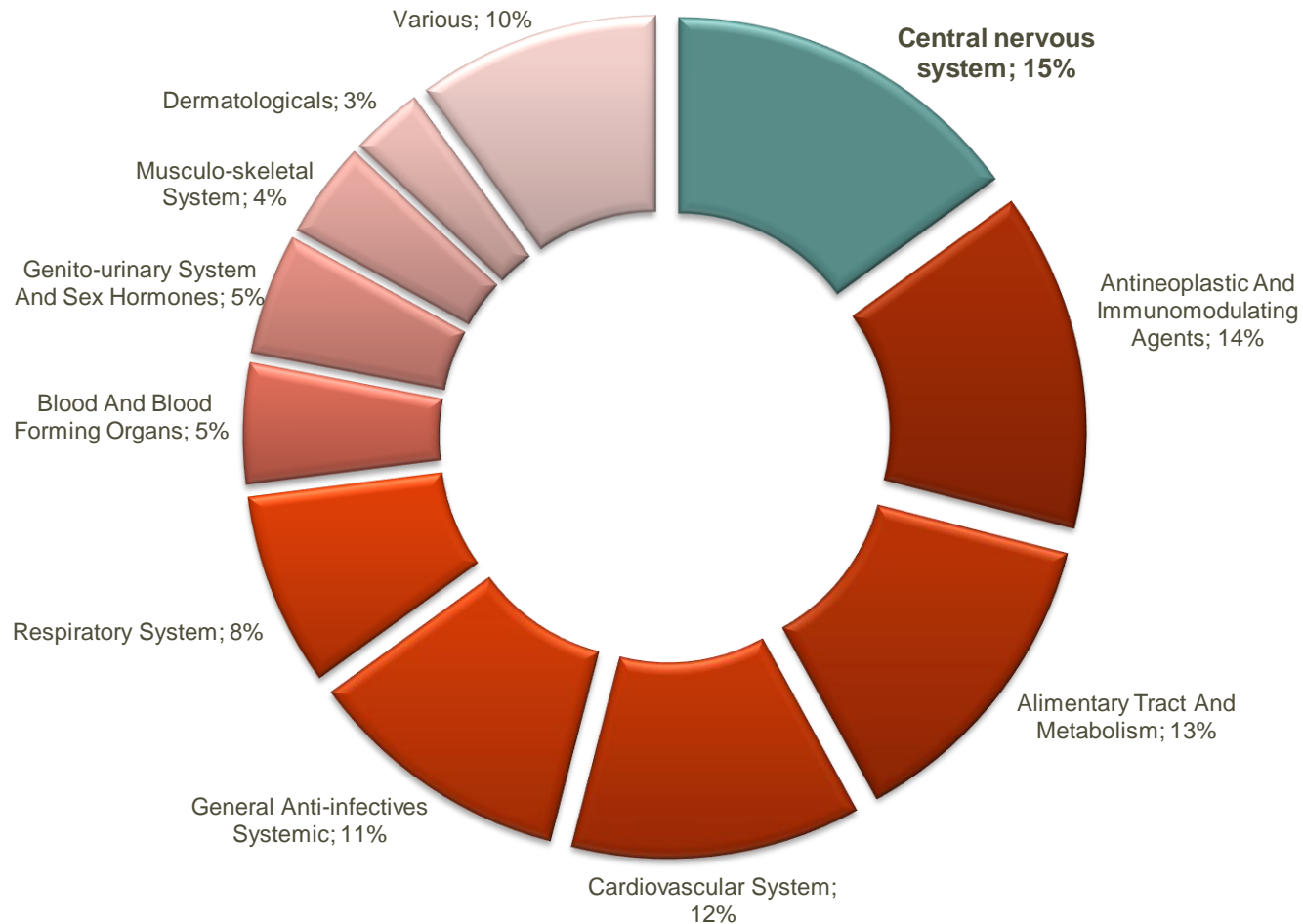
## Appendix

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- ★ Lundbeck overview
- ★ Commercial operations
- ★ Pipeline
- ★ Financials
- ★ **The CNS market**
- ★ The Lundbeck share

# Worldwide pharmaceutical market 2012

## USD 857 billion (-1%)



# CNS market overview (2012)

	Market size (2012)				Market leaders (2012)	
	Value (USDbn)	Growth	# of patients*	Unmet medical needs	Compound	Share (value)
Total pharma	857	-1%	-	-	-	-
Total CNS	128	-5%	-	-	-	-
Alcohol (N7E)	0.287	13%	5% of men and 1.4% of women in Europe	<ul style="list-style-type: none"> <li>• Greater resources – number of treatment facilities and trained physicians is inadequate</li> <li>• The integration of alcohol treatment into primary care</li> <li>• Improved effectiveness</li> <li>• Improved compliance</li> </ul>	1. Campral 2. Vivitrol 3. Antabuse	\$61m \$58m \$13m
Anti-Alzheimer's (N7D)	6.7	-12%	>7 million <sup>2</sup>	<ul style="list-style-type: none"> <li>• Disease modifying treatment</li> <li>• Disease slowing agents</li> <li>• Improved symptomatic treatments</li> <li>• Longer lasting symptomatic treatments</li> </ul>	1. Memantine 2. Donepezil 3. Rivastigmine 4. Galantamine	41% 31% 20% 7%
Antidepressants (N6A)	19	-9%	~40 million <sup>2</sup>	<ul style="list-style-type: none"> <li>• Drugs with higher remission rates</li> <li>• Increased onset of action</li> <li>• Current therapies are relatively well-tolerated but still room for improvement especially on sexual side effects</li> </ul>	1. Duloxetine 2. Escitalopram 3. Venlafaxine 4. Paroxetine	32% 18% 8% 6%
Anti-Parkinson's (N4A)	4.3	-1%	>3 million <sup>2</sup>	<ul style="list-style-type: none"> <li>• Therapies that provide neuroprotection and/or neurorestoration</li> <li>• An optimal trial design for demonstrating neuroprotection and/or neurorestoration</li> <li>• Control of levodopa-induced motor response complications</li> </ul>	1. Levodopa 2. Pramipexole 3. Rasagiline 4. Stalevo 5. Ropinirole	20% 20% 14% 12% 11%
Antipsychotics (N5A)	22.9	-20%	Approx 1% of global population	<ul style="list-style-type: none"> <li>• Improved treatment of cognitive dysfunction</li> <li>• Improved treatment of negative symptoms</li> <li>• Improved treatment of co-morbid depression and anxiety</li> <li>• Early stage, definitive diagnostics</li> </ul>	1. Aripiprazole 2. Quetiapine 3. Olanzapine 4. Risperidone	36% 24% 12% 9%

Sources: IMS Knowledge Link 2013 (Market size), IMS data 2013 (Market leaders)

\*2011 numbers

Growth, 12 months to Q4 2012/2011, \$(%)

NOT FOR PROMOTIONAL USE

# CNS market size – overview (2012)

	Total market		USA		Europe		Int. Markets	
	Value (USDbn)	Growth	Share	Growth	Share	Growth	Share	Growth
Total pharma	857	-1%	38%	-1%	26%	-7%	36%	4%
Total CNS	128	-5%	47%	-7%	25%	-10%	27%	4%
Alcohol	0.3	14%	33%	14%	32%	-6%	36%	41%
Anti-Alzheimer's	6.7	-12%	38%	-12%	26%	-21%	36%	-3%
Antidepressants	18.8	-9%	51%	-13%	22%	-11%	28%	0%
Anti-epileptics	14.6	2%	41%	3%	30%	-5%	29%	10%
Anti-Parkinson's	4.3	0%	22%	8%	45%	-6%	30%	3%
Antipsychotics	22.9	-20%	58%	-26%	22%	-19%	20%	3%
Fibrinolytics (incl. stroke)	1.1	11%	51%	16%	24%	1%	26%	10%

Source: IMS Health Knowledge Link 2013& IMS Syndicated Analytics Library 2013 (Audited sales)

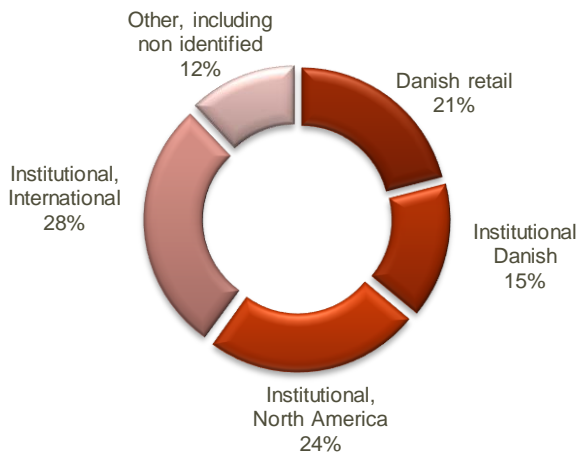
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# The Lundbeck share

## Composition of free float ownership (end 2012)



- ★ Free float in the Lundbeck share is 30%
  - ★ The Lundbeck Foundation holds 70% of the total share capital
- ★ Free float (approximately 60m shares) is traded approx. once over annually

LUNDBECKFONDEN

- ★ The Lundbeck Foundation is a commercial foundation established in 1954 by Grete Lundbeck, widow of the founder of H. Lundbeck A/S
- ★ The main objective of the Lundbeck Foundation is to
  - ★ Maintain and expand the activities of the Lundbeck Group
  - ★ Provide financial support for research of the highest quality in biomedical and natural sciences

# Sponsored ADR programme

- ★ Lundbeck has established a sponsored Level I ADR programme in the US. The ADRs trade on the premier tier of Over-The-Counter (“OTC”) market in the US. Details are as follows:

<b>Ticker Symbol</b>	<b>HLUYY</b>
CUSIP	40422M206
Ratio	1 ADR : 1 Ordinary Shares
ADR depositary	Deutsche Bank



**Deutsche Bank**

- ★ Please contact the Deutsche Bank’s dedicated ADR broker desks:

Jay Berman (New York)

Tel: +1 212 250 9100

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Tel: +44 20 7547 6500

Email: [simon.davies@db.com](mailto:simon.davies@db.com)



# For more information please contact Investor Relations

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## Share information

Lundbeck's shares are listed on the stock exchange in Copenhagen under the symbol "LUN".

Lundbeck has a sponsored Level 1 ADR programme listed in the US (OTC) under the symbol "HLUYY".

For additional company information, please visit Lundbeck at: [www.lundbeck.com](http://www.lundbeck.com)

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