Newron Pharmaceuticals S.p.A.

R&D/Business Update

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Overview

- Focus on global CNS and pain markets, addressing diseases with significant unmet medical needs
- Late-stage validated clinical pipeline
- Proven drug discovery expertise
- Management with proven track record of bringing CNS drugs to market (Comtan™, Cabaser™, Exelon™, Clozaril™)
- Pipeline expanded through acquisition of neuro-inflammation company Hunter-Fleming, April 2008
- Operations in Bresso (I), Basel (CH) and Bristol (UK)
- Listed on main segment of SIX Swiss Exchange (NWRN)

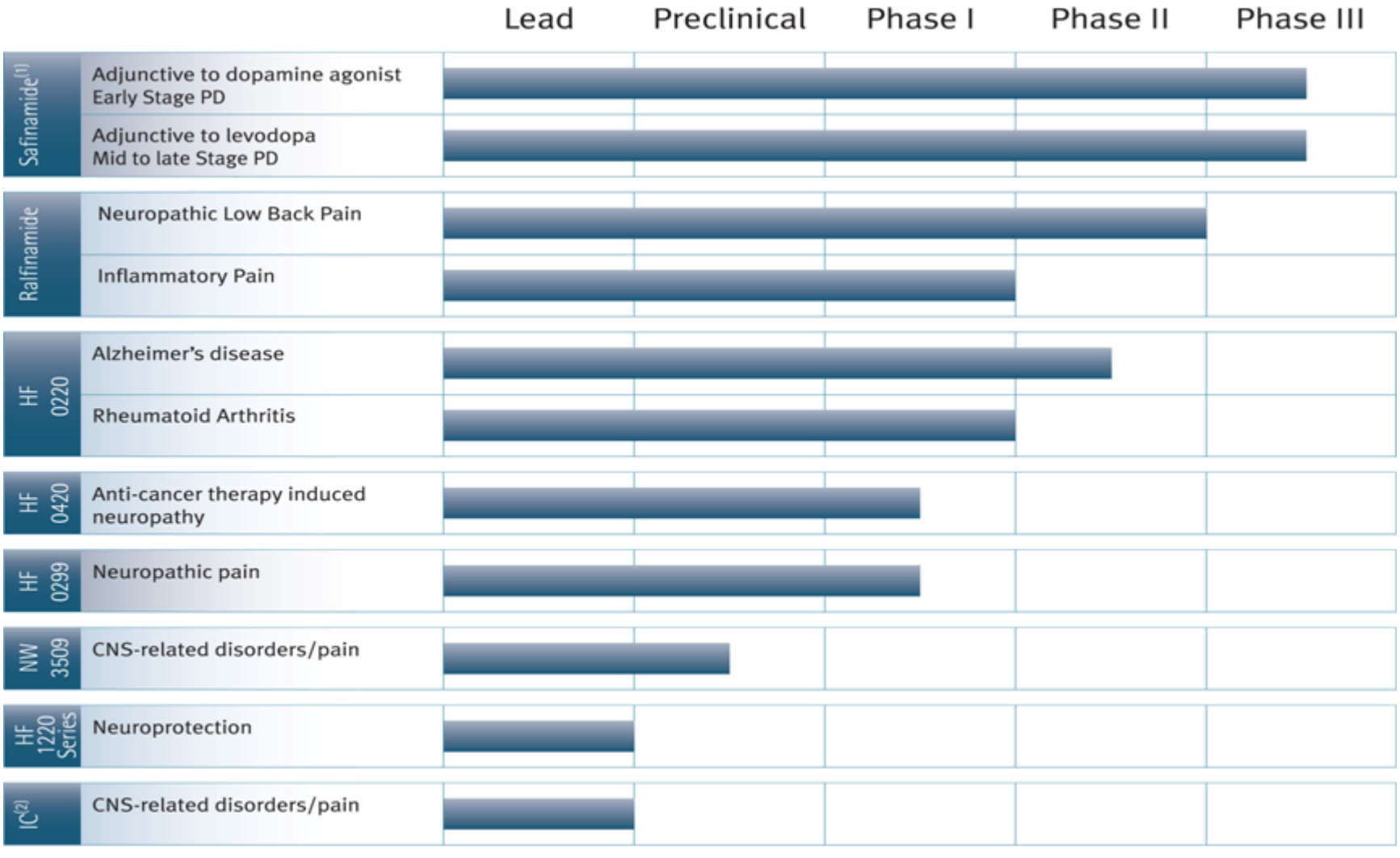
Recent Milestones

- Positive ralfinamide Phase II data in Neuropathic Pain
- Exciting Phase II results with ralfinamide in NLBP
- EPO grant two new patents on safinamide significantly extending its use:
  - Safinamide plus L-dopa therapy in PD until 2024
  - Safinamide in RLS until 2025
- Completion of patient enrolment in Phase III clinical trial with safinamide in mid-to-late stage Parkinson's disease
- Acquisition of Hunter-Fleming Ltd.
- Positive Phase II safety and tolerability results for HF-0220 in Alzheimer's disease
- Appointment of senior industry experts as non-executive Members of the Board of Directors
- Inclusion into Swiss Performance Index and SXI indices
- €5m Italian government R&D grant

Hunter-Fleming: right deal, right price

- Stock purchase agreement signed 9 February, 2008
- Providing for the acquisition of 100% of HF issued share capital
- Newron shareholders' approval April 24, 2008
- Transaction closed May 13, 2008
- €4.7m paid upfront for the fully diluted share capital of Hunter-Fleming, in newly issued Newron shares (3.1 % holding in Newron)
- End of 6 month lock-up October 23, 2008
- Newron to pay success-based milestone payments relating to further progression of the HF programs, up to a maximum of €17m

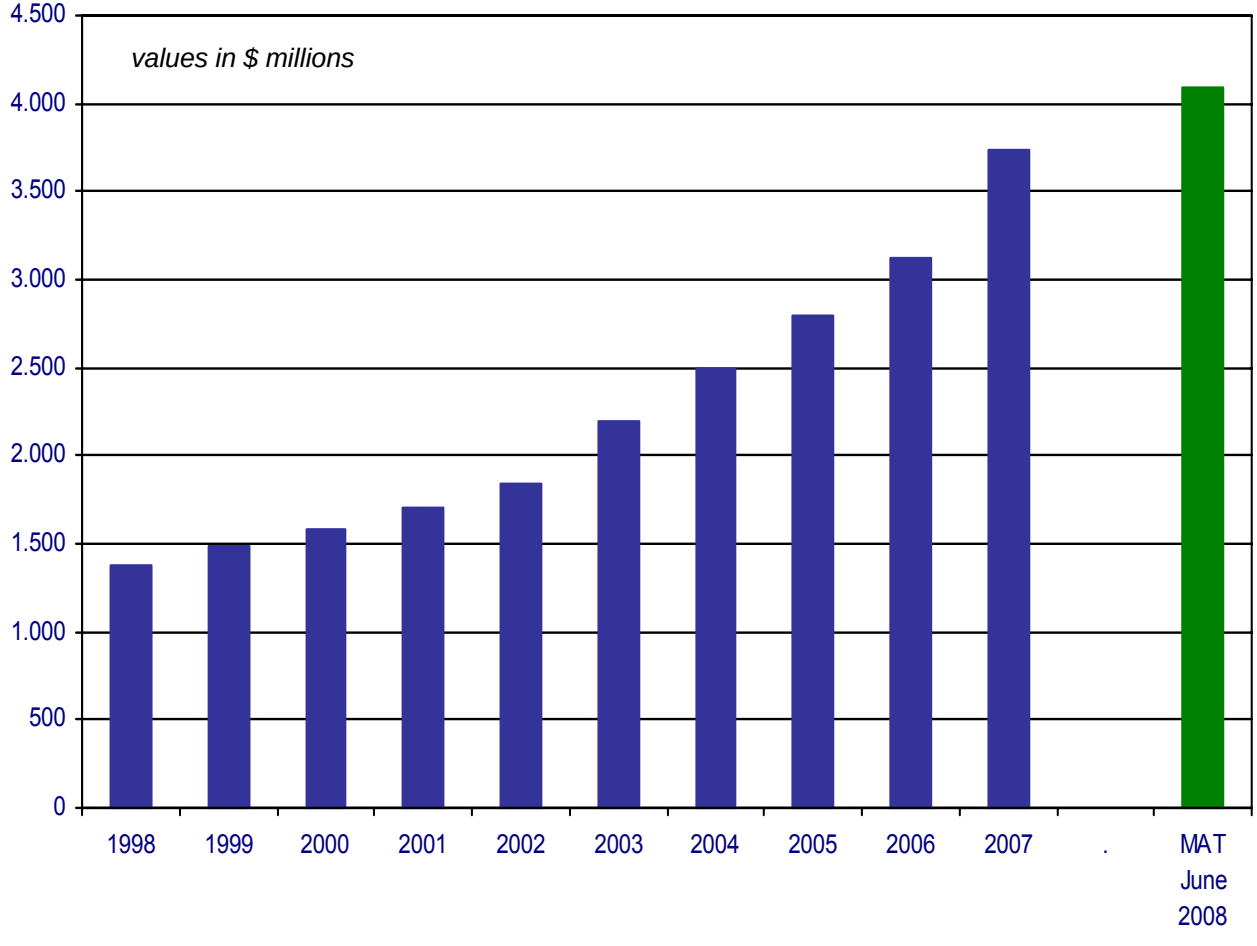
Broad and diversified pipeline



(1) Newron is undertaking Phase III trials with safinamide for the treatment of PD on behalf of its partner Merck Serono
(2) IC = Ion Channel Program
(3) HF 1020 in preclinical development for asthma is part of Newron's equity holding in Trident

Safinamide

Parkinson's Disease drug market trend



Uninterrupted increase of the market value over the last several years with double digit growth since 2003

Market value driven by highly priced dopamine agonists with about 50% market share

Rx volumes still dominated by low priced levodopa

Safinamide

- Once a day oral adjunctive therapy for any stage of PD
- Unique mechanism of action
  - Enhancement of dopaminergic function
  - Reduction of glutamatergic activity
- Small molecule, high bioavailability
- Currently in Phase III development for PD with partner Merck Serono
- Potential in cognitive disorders
- New patents granted significantly extend protection in EU
  - Add-on to L-dopa patent
  - Use patent for RLS

… with potential benefits in Parkinson's disease (target product profile)

Current PD paradigm

Early stage (mild) → Late stage

Dopamine agonist

- First-line treatment in early patients, efficacy decreases over time, significant side-effects

Levodopa + adjunct

- Associated with dyskinesia and other major side effects

Safinamide enhances existing treatment paradigm

Early stage (mild) → Late stage

Dopamine agonist

Dopamine agonist + safinamide

- Enhances dopamine agonist effects
- Delays levodopa use
- Improves cognition

Levodopa + (adjunct +) safinamide*

- Improves "on" time, reduces "off" time
- Improves dyskinesias
- Reduces levodopa dose
- Improves cognition

* as suggested by earlier studies and mechanism of action

**Delay the use of levodopa as long as possible;
once you use levodopa, dose as low as possible**

Long-term safety and efficacy of safinamide added to dopamine agonists in early PD
Study 015 / 017

Study 015 / 017: study design

- Multinational, double-blind, placebo-controlled Phase III study to determine the efficacy and safety of safinamide
- Safinamide administered as add-on therapy to a stable dose of a single DA
- Patients with early idiopathic PD (< 5 years) could be treated for 18 months
  - Patients were initially treated for 6 months (Study 015) and eligible patients could enter the 12-month extension (Study 017)
- Treatment arms
  - DA + safinamide 50-100 mg/day (n=90)
  - DA + safinamide 150-200 mg/day (n=90)
  - DA + placebo (n=90)

Study 015 / 017: endpoints

Study 015

- Primary: change in UPDRS part III scores from baseline using hierarchical analysis

Study 017

- Primary: time to intervention from baseline (Day 0 of Study 015)
  - Increase in DA dose
  - Addition of another DA or other PD therapy
  - Discontinuation due to lack of efficacy
- Secondary endpoints included: change in UPDRS part III scores from baseline and responder rate (≥30% decrease in UPDRS part III score)

UPDRS: Unified Parkinson's Disease Rating Scale; UPDRS part III, motor score

Study 015: key efficacy results

- 6 month data indicated that safinamide 50-100 mg/day was significantly superior to DA monotherapy

Measure	Safinamide 50-100 mg/day	Safinamide 150-200 mg/day	Placebo
UPDRS part III (mean change, ITT / MLM)	-6.0 ± 7.2*	-3.9 ± 6.0	-3.6 ± 7.1
UPDRS part III (responder rate)	38.2%*	36.8%*	24.7%
UPDRS part II	-2.2 ± 3.8*	-1.4 ± 2.7	-1.2 ± 2.5

*p<0.05 vs placebo

- Analysis of cognitive function in a subset of patients showed significant benefits of safinamide in working memory, executive function and reaction time

Response defined as ≥30% decrease in UPDRS part III score;
ITT, intent to treat; MLM, mixed linear model; UPDRS part II, activities of daily living

Study 015: key safety results

- Safinamide was well tolerated
- Discontinuation rates were: 10% for safinamide 50-100 mg/day; 21% for safinamide 150-200 mg/day; and 21% for placebo
- Safinamide was not associated with any statistically significant or clinically notable changes in AE's or other safety measurements

Study 017: patient disposition

Patients, n (%)	Safinamide 50-100 mg/day (n=90)	Safinamide 150-200 mg/day (n=89)	Placebo (n=90)
Randomized in Study 015	90 (100%)	89 (100%)	90 (100%)
Completed 6 months	81 (90%)	70 (78.7%)	81 (90%)
Entered Study 017	80 (100%)	69 (100%)	78 (100%)
Completed Study 017	64 (80%)	61 (88.4%)	62 (79.5%)

Study 017: reasons for discontinuation

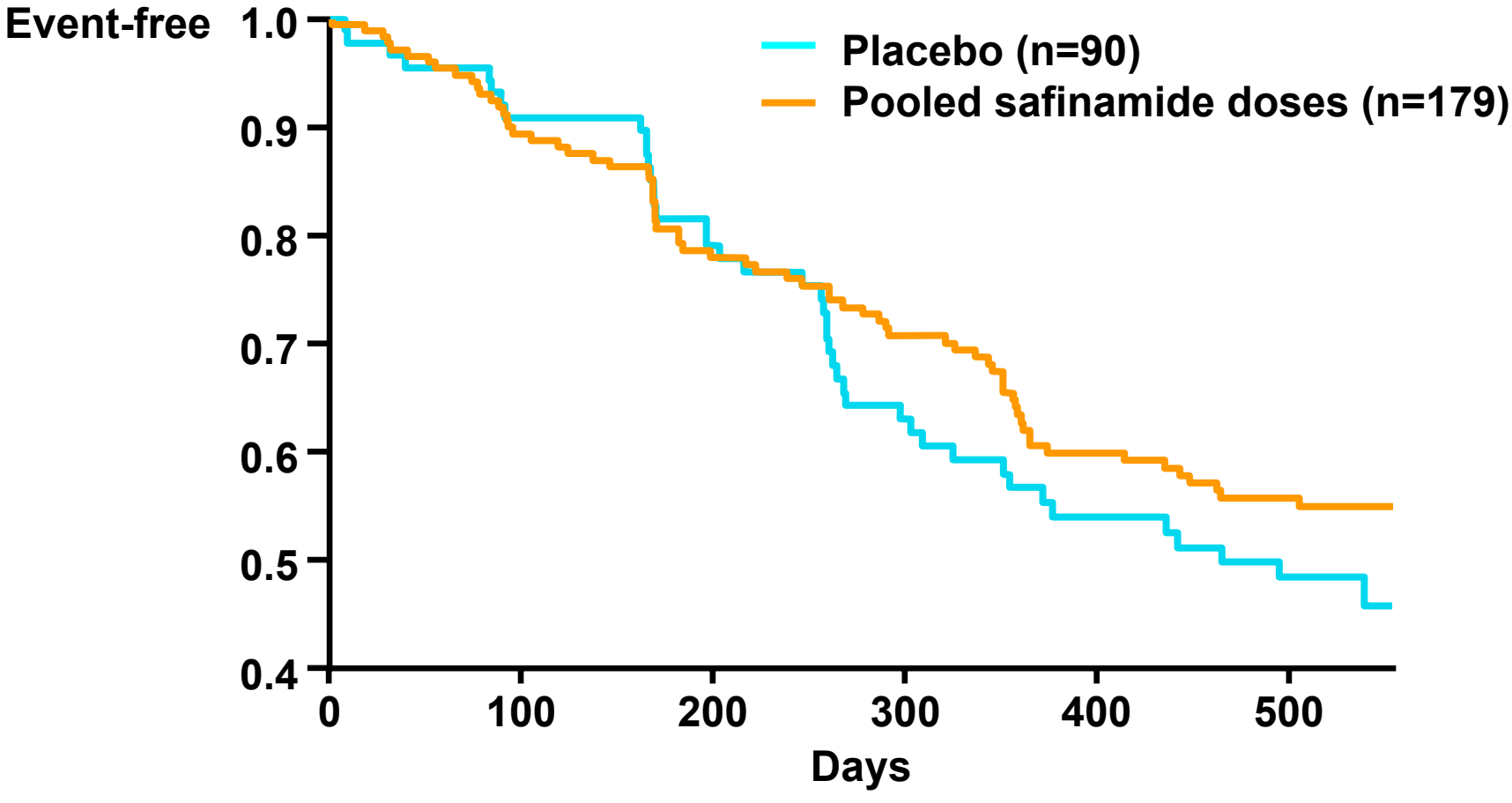
Reason for discontinuation, n (%)	Safinamide 50-100 mg/day (n=80)	Safinamide 150-200 mg/day (n=69)	Placebo (n=78)
Withdrawal of consent	8 (10.0)	3 (4.3)	5 (6.4)
Lack of efficacy	2 (2.5)	4 (5.8)	5 (6.4)
Non-serious AEs	1 (1.3)	1 (1.4)	2 (2.6)
Serious AEs	2 (2.5)	0	1 (1.3)
Lost to follow-up	2 (2.5)	0	1 (1.3)
Death	0	0	1 (1.3)
Other	1 (1.3)	0	1 (1.3)
Total	**16 (20.0)**	**8 (11.6)**	**16 (20.5)**

Study 015 / 017 time to intervention*: statistical assumptions

- The two safinamide dose groups were pooled for the analysis of time to intervention, based on the assumption that both safinamide dose groups would be superior to placebo
- Expected proportions of patients requiring an intervention over 18 months
  - Placebo: 75%
  - Safinamide: 55%
  - Constant hazard ration: 0.4812
  - Power: 90% to detect 20% difference at 5% chance level

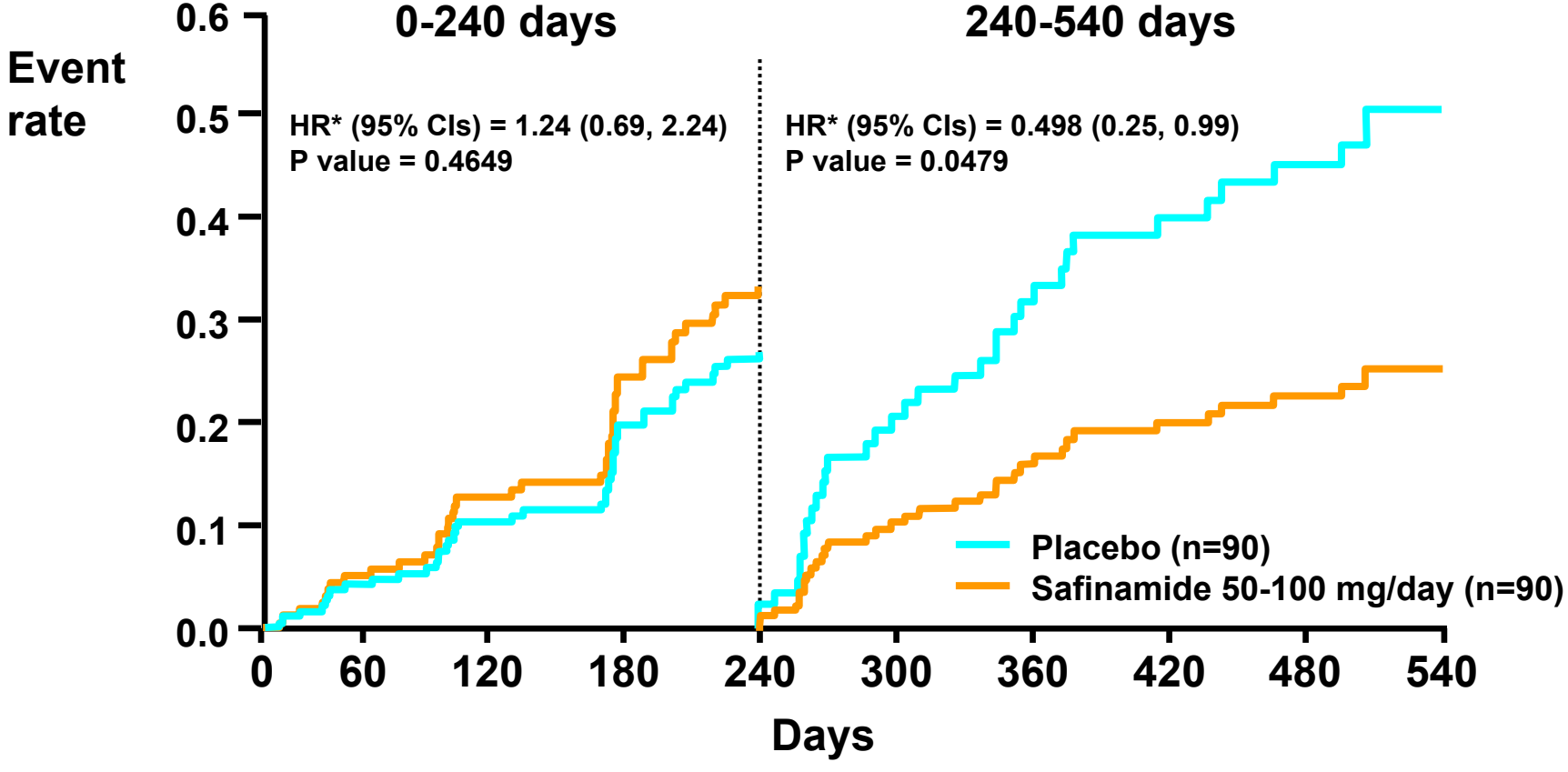
***Time to intervention defined as increase in DA dose, addition of another DA or other PD therapy such as L-dopa or discontinuation due to lack of efficacy**

Time to intervention Kaplan-Meier analysis



Pooled safinamide groups demonstrated a non-significant delay to intervention of 93 days (p=0.33 vs placebo)

Time to intervention: post-hoc analysis of safinamide 50-100 mg/day vs placebo (Cox reg. model)



Only 25% of patients receiving safinamide 50-100 mg/day required intervention after >240 days of treatment, compared with 51% of placebo patients (p<0.05)

***Aalen Nelson estimates of the cumulative hazard function**

Study 017: UPDRS part III 18 month data

	Safinamide 50-100 mg/day	Safinamide 150-200 mg/day	Placebo
UPDRS part III (mean change, MLM)	-4.70 ± 9.3*	-1.29 ± 8.5	-1.95 ± 7.4
Responder rate (%)	42.5 (34/80)*	27.5 (19/69)	24.4 (19/78)

Response defined as ≥30% decrease in UPDRS part III score
***p<0.05 vs placebo**

Study 017: conclusions

- Safinamide was generally well tolerated during 18 months of treatment
- Safinamide was associated with a delay to treatment intervention of ~90 days
- Safinamide 50-100 mg/day was associated with significant improvements compared with DA-agonist monotherapy
  - Reduction in rate of intervention (25% vs 51% with placebo; $p<0.05$)
  - Reduction in UPDRS part III scores (-4.70 vs -1.95 with placebo; $p<0.05$)
  - Increase in responder rate (42.5% vs 24.4% with placebo; $p<0.05$)
- Longer studies with at least 200 patients per treatment group are needed to demonstrate a significant benefit in *a priori* time to intervention analyses

Add-on to L-dopa in mid-to-late stage PD (Study 016)

- Pilot Phase II trial showed benefit of safinamide in L-dopa treated patients
- Phase III, multicenter, multinational (Europe, Asia) on-going
- 669 patients in mid-to late stage PD, with motor fluctuations
- 6 months plus 18 months extension
- 50 and 100 mg/day doses vs. placebo (L-dopa)
- Primary efficacy endpoint after 6 months: Increase in mean daily on-time
- Further efficacy measures: improvement in cognition, reduction of dyskinesia
- Enrollment completed May 2008
- Top line results early 2009

Promising results in cognition

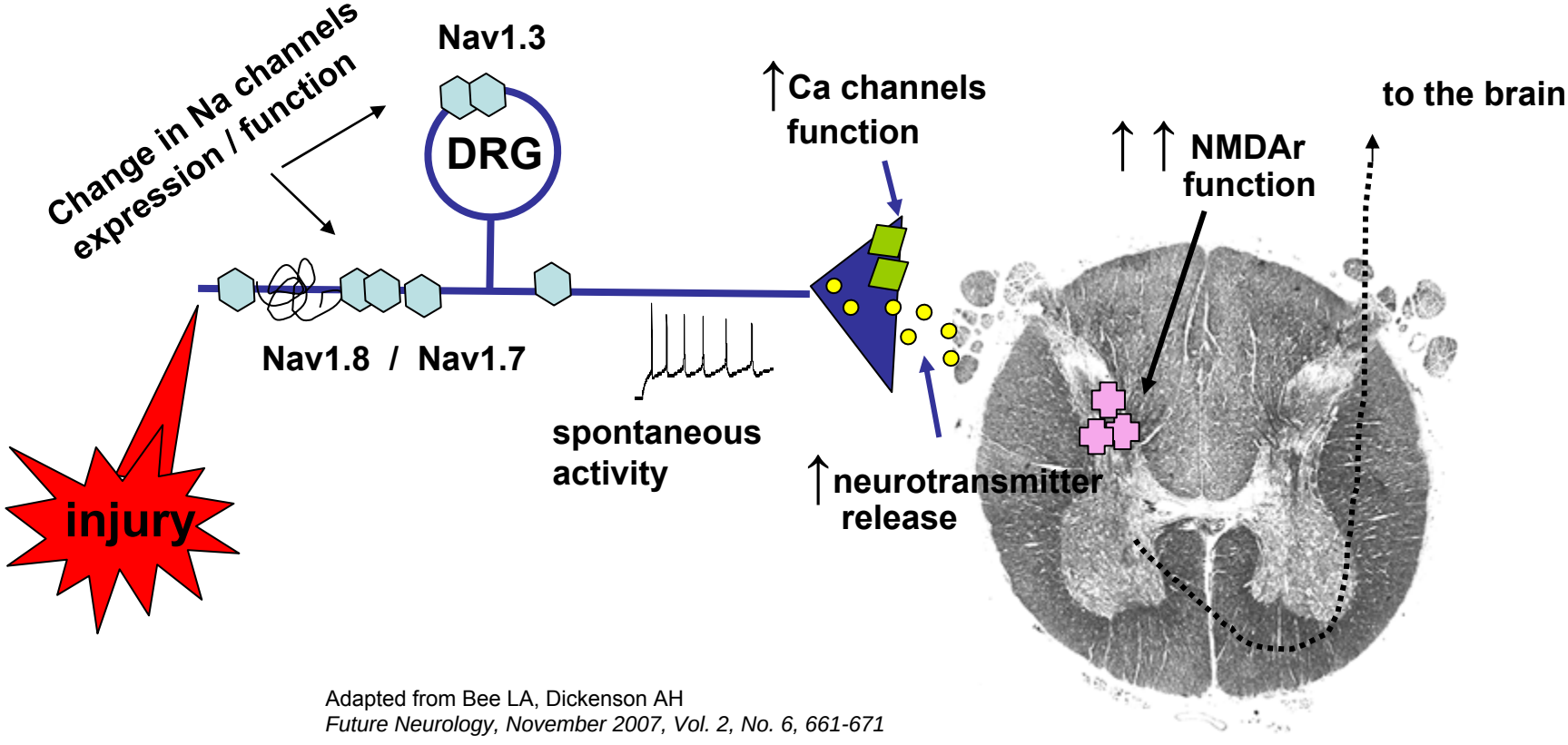
- Cognitive effects seen as early as 12 weeks after starting safinamide treatment
- Statistically significant improvement of two major cognitive domains often impaired in early stage PD (executive functioning and working memory)
- Full data presented at the Movement Disorder Society's 11th International Congress – Istanbul on 7 June 2007
- Safinamide offers the opportunity to be explored in multiple cognitive disorders
- Huge market opportunity beyond cognition in PD
  - Age Associated Memory Impairment (AAMI, 13M in US)
  - Mild Cognitive Impairment (MCI, 10 -15% diagnosed with AD each year)
  - Alzheimer's disease (4.5M in US; 14M in 2030)

Ralfinamide

Ralfinamide: an innovative therapeutic agent for Neuropathic Low Back Pain

- Oral use, small molecule, new chemical class
- Modulation of Na, Ca, NMDA receptors: key targets for the control of pain transmission
- Potent inhibitor of Na(v)1.7 channel
- Long-lasting anti-allodynic and anti-hyperalgesic effects in models of neuropathic and inflammatory pain
- No development of tolerance on chronic dosing
- No need for titration
- Demonstrated efficacy in placebo-controlled trial in patients with peripheral neuropathic pain
- First in-class agent for the treatment of NLBP

Peripheral and central changes in NP pain



Adapted from Bee LA, Dickenson AH
Future Neurology, November 2007, Vol. 2, No. 6, 661-671

Na (v) 1.7 channel

- Located in peripheral neurons
- Plays an important role in action potential production in these cells
- Recent genetic studies have identified Na(v) 1.7 dysfunction in three different disorders
- Gain-of-function mutations cause primary erythermalgia and paroxymal extreme pain disorder
- Non-sense mutation results in loss of function and a condition known as channelopathy associated insensitivity to pain

Ralfinamide is a potent blocker of Na(v)1.7 channel

Expert Opin. Ther. Targets (2007) 11(3):291-306

Table 2. Preclinical potency, efficacy and clinical dose data for oral sodium channel blockers.

Drug	Status	$Na_V1.7$ potency (K_i)‡	Rodent efficacy model* MED	Clinical efficacy for neuropathic pain Dose	Plasma concentration	Efficacy
Lidocaine	Transdermal formulation approved	16 µM [172]	10 – 30 mpk i.v.	5 mpk i.v.	4 – 20 µM	+
Mexiletine	No pain indication	11 µM§	30 – 100 mpk p.o.	400 – 1200 mg	4 µM	+ –
Carbamazepine	Approved for TN	29 µM [172]	100 mpk p.o.	200 – 800 mg	20 – 50 µM	+
Oxcarbazepine	Phase III	?	10 – 100 mpk p.o.	300 – 1800 mg	20 – 60 µM	+
Lamotrigine	Phase III	34 µM [172]	30 mpk p.o	400 mg	2 µM	+ –
4030W92	Discontinued	1.7 µM§	?	25 mg	?	–
Ralfinamide	Phase II	0.6 µM§	0.1 mpk p.o	80 – 320 mg	?	+

*Neuropathic pain model (i.e., spinal nerve ligation, partial sciatic nerve ligation, or chronic construction injury). ‡Affinity for inactivated channels.
§Priest BT, unpublished reuslts. i.v.: Intravenous; MED: Minimal efficacious dose; p.o.: per os; TN: Trigeminal neuralgia.

Phase II in neuropathic pain

- Multi-centre, randomised, D-B, placebo-controlled, flexible ascending dose (80-320mg/day) study
- Indication: Mixed Neuropathic Pain Syndromes
- Randomization: Unequal; ralfinamide vs placebo 2:1
- 272 patients
- Treatment duration: 8 weeks
- Countries: Austria; India; Italy; Poland; Czech-R; UK
- Primary efficacy measure: VAS score

Ralfinamide is well tolerated: side effects comparable to placebo

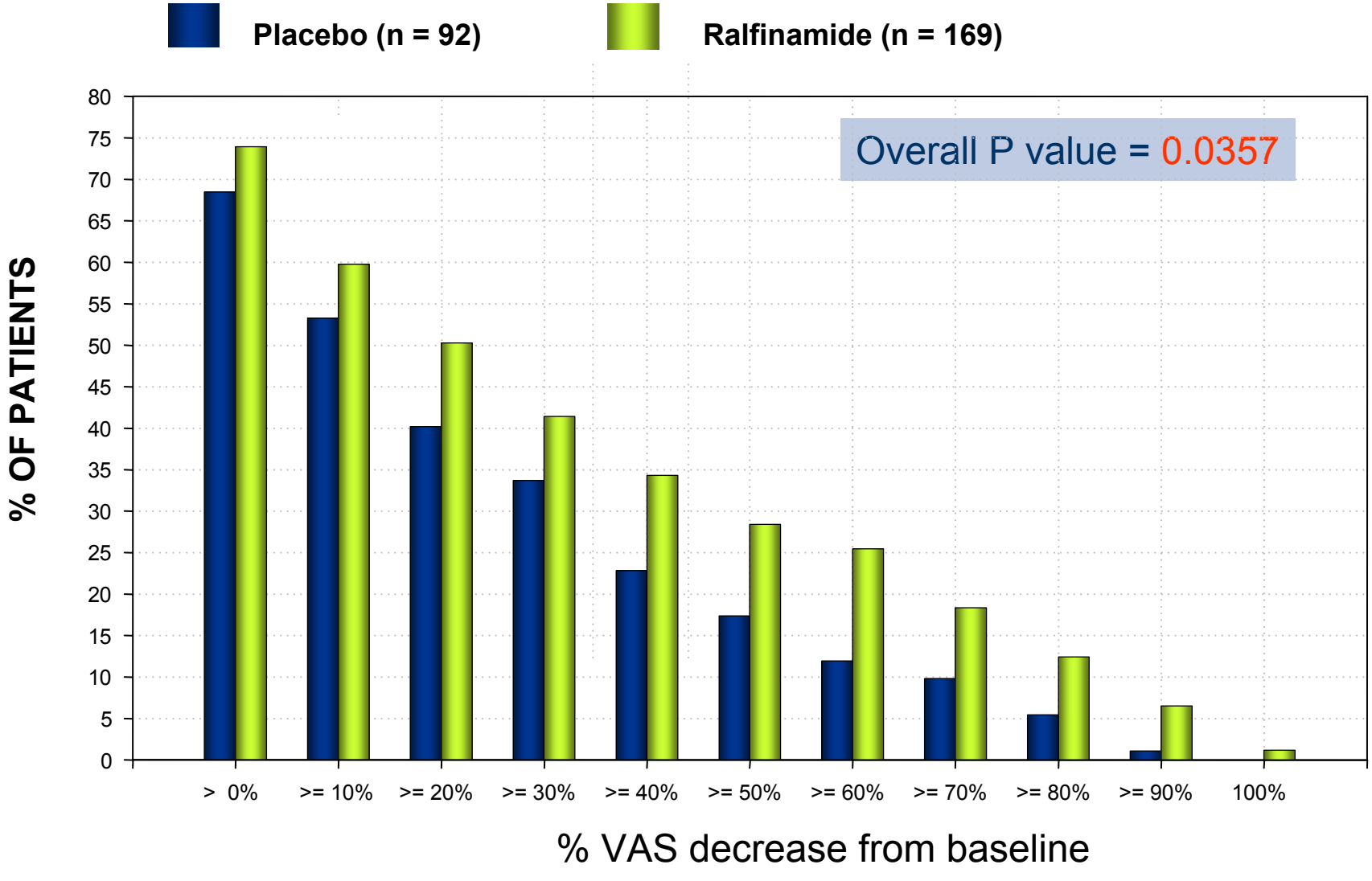
- Ralfinamide was well tolerated with no evidence of any statistically significant or clinically relevant pattern of change compared to placebo
- Highest dose (320 mg/day BID) reached in 81.4% of patients, with about 75% of patients maintaining the dose
- Side effects:

	ralfinamide	placebo
– Headache	15.3%	17.9%
– Dizziness	5.1%	13.7%
– Nausea	6.8%	10.5%
– Dyspepsia	5.1%	8.4%
– Diarrhea	4.5%	6.3%
– Dry mouth	5.7%	2.1%

Phase II results in NP: efficacy

- Clear evidence of efficacy in a mixed population with peripheral NP
- Positive effect seen both as change vs baseline as well as 50% responder rate on:
  - VAS
  - Likert (Pain)
  - Daily Diary Sleep
  - Daily Diary Activity

VAS (% reduction by treatment): significant increase in responder rates



Secondary efficacy measures (LOCF): proportion of patients with ≥ 1 point decrease in daily diary - baseline to end point

≥ 1 point decrease in: %(n)	Placebo N=74	Ralfinamide N=126	All Patients N=200	P-value (A)
Daily Pain Score	40.5 (30)	58.7 (74)	52 (104)	0.013 *
Sleep Score	29.7 (22)	50.8 (64)	43 (86)	0.004 *
Activity Score	36.5 (27)	53.2 (67)	47 (94)	0.02 *
Burning Pain Score	32.4 (24)	44.4 (56)	40 (80)	0.09 (*)
Shooting Pain Score	31.1 (23)	47.6 (60)	41.5 (83)	0.02 *
Touch/ Location/ Hypersensitivity Score	33.8 (25)	42.1 (53)	39 (78)	0.25

*p=<0.05;

N: Number of patients. n: Patients with data available. %: Percentage based on N.
(A) Treatments compared using a Cochran-Mantel-Haenszel test.

Ralfinamide in Nerve Compression & Entrapment

- A large subgroup included in Phase II study (96 out of 272)
- Clinically meaningful and statistically significant benefit measured as
  - VAS
  - Likert (Pain)
  - Daily Diary Sleep
  - Daily Diary Activity

NCET: Anatomical/Etiological classification

- Diseases characterized by painful focal neuropathies (mono neuropathies, plexopathies and radiculopathies)
  - Carpal tunnel syndrome
  - Tarsus tunnel syndrome
  - Ulnar nerve entrapment
  - Compression radiculopathy
  - Lumbar spinal stenosis
  - Sciatic nerve compression
  - Spinal root compression
  - Intercostal neuralgia

Responder analysis: proportion of patients with a VAS decrease of at least 30% or 50% - NCET (ITT-LOCF)

VAS Responder rate LOCF	Nerve Compression/Entrapment - ITT			
	30%		50%	
Treatment	Ralfinamide	Placebo	Ralfinamide	Placebo
N	57	39	57	39
Proportion of responders n (%)	31 (54.4)	13 (33.3)	26 (45.6)	8 (20.5)
Odds ratio	2.38		3.25	
95% CI for odds ratio	1.02, 5.55		1.27, 8.29	
P-Value (A)	0.043 *		0.012 *	

*p=<0.05

N: Number of patients. n: Patients with data available. %: Percentage based on N.
Not Est: Not estimable due to insufficient patient numbers.
(A) Treatments compared using a Cochran-Mantel-Haenszel test.

Responder analysis: Likert pain (proportion of patients with a decrease of at least 30% or 50%) – NCET (ITT-LOCF)

Responder rate LOCF	Nerve Compression/Entrapment - ITT			
	30%		50%	
Treatment	Ralfinamide	Placebo	Ralfinamide	Placebo
N	57	39	57	39
Proportion of Responders n (%)	33 (57.89)	14 (35.90)	24 (42.11)	7 (17.95)
Risk Difference (95% CIs)	22.0 (2.2, 41.8)		24.2 (6.6, 41.7)	
Chi-Square P-value (A)	0.0342 *		0.0129 *	

*p=<0.05

(A) The treatments were compared using a Chi-Square test. CI = confidence interval, N = number of patients, (%) percentages based on N

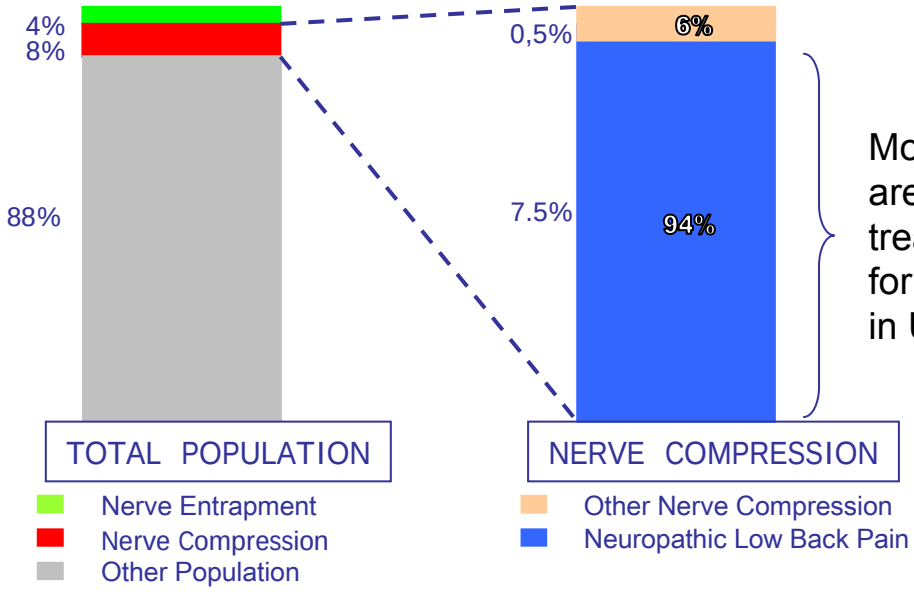
Responder analysis: Likert pain (patients with 2 or more point improvement) - NCET (ITT-LOCF)

Responder rate LOCF	Nerve Compression/Entrapment	
Treatment	Ralfinamide	Placebo
N	57	39
Proportion of Responders n (%)	31 (54.4)	11 (28.2)
Odds Ratio (95% CI for Odds Ratio)	3.03 (1.27, 7.25)	
P-value (A)	0.012 *	

*p=<0.05

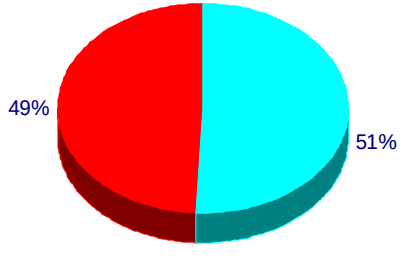
N: Number of patients. n: Patients with data available. %: Percentage based on N. Not Est: Not estimable due to insufficient patient numbers. Responder: Patient with a 2 or more point improvement in Mean Daily Pain Score on the Likert Scale.
(A) Treatments compared using a Cochran-Mantel-Haenszel test.

Nerve Compression: patient potential for ralfinamide

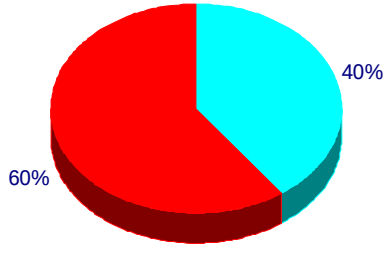


More than 55 million patients are potential candidates for treatment with ralfinamide for Neuropathic Low Back Pain in US, EU and JP

Patient prevalence



Diagnoses



All Other Neuropathic Pain Neuropathic Low Back Pain

All Other Neuropathic Pain Neuropathic Low Back Pain

Ralfinamide in NLBP

- Prevalence of NCET is about 12% (8% for nerve compression)
- NLBP is the most common clinical emergence of nerve compression (>95%)
- No drugs are approved for NLBP
- Ralfinamide could be the first approved drug for NLBP
  - Potential for premium pricing
  - Fast market penetration
- Phase IIb/III in NLBP to be started
- Blockbuster opportunity

Comparability of response to Ralfinamide in patients diagnosed with NCET vs NLBP

50% Responder rate LOCF	NCET – ITT		NLBP - ITT	
Treatment	RALF	PBO	RALF	PBO
N	57	39	33	21
Proportion of responders n (%)	26 (45.6)	8 (20.5)	11 (33.33)	2 (9.52)
Difference	25.1		23.8	
P-Value	0.012 *		0.0460 *	

NLBP Study Design

- Double-blind placebo controlled, parallel-group, multinational trial
- Treatments:
  - Placebo and 2 doses of ralfinamide
- Randomisation: Equally to all three groups
- Study Duration: 12 weeks
  - Patients who complete 12 weeks of treatment will be eligible to enter a double-blind 40 week extension
  - Patients will continue on the same dose of study medication they were receiving at the end of the 12 week treatment period
- Number of Patients: approx 400

NLBP Diagnostic Criteria

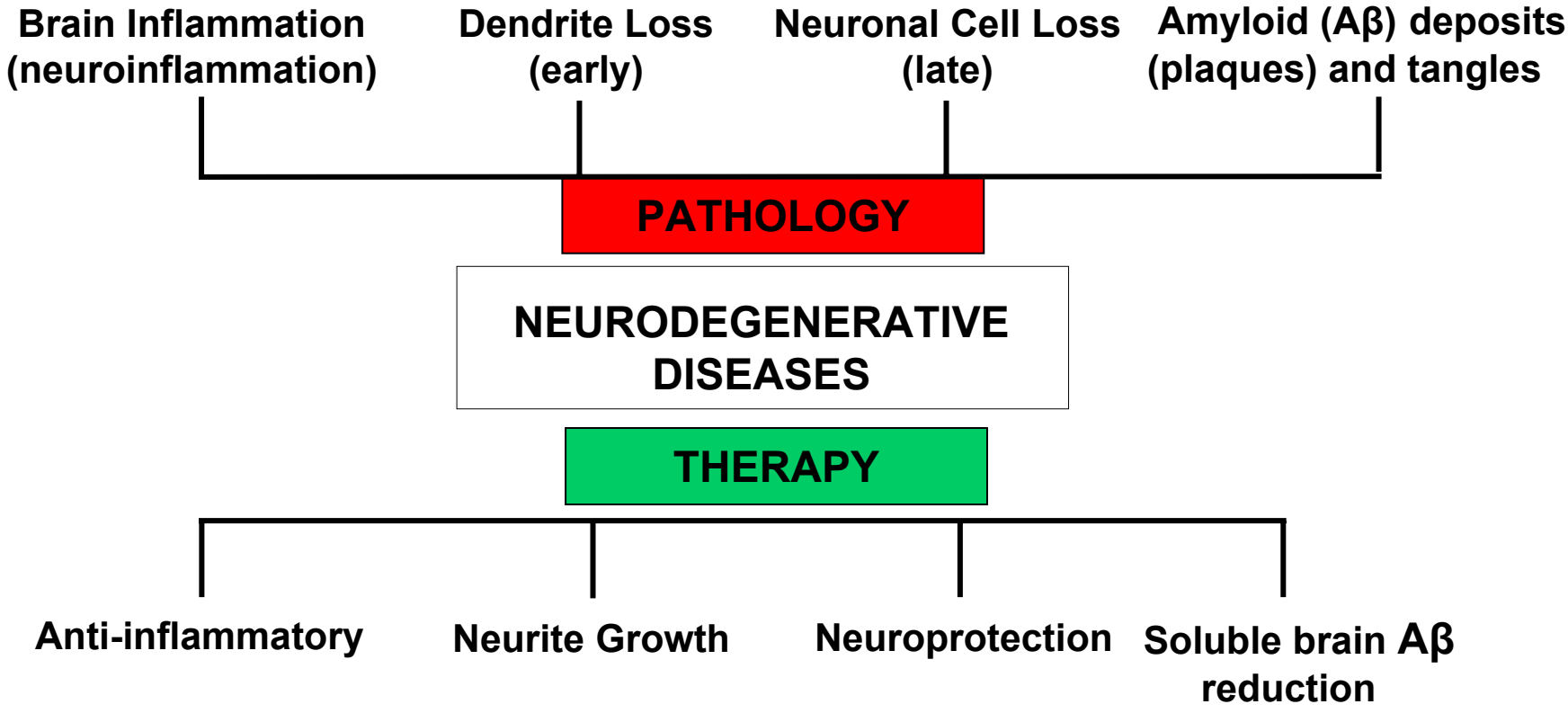
- At least moderate (>40mm) pain as judged by patients' self ratings on the VAS
- Present for at least 3 months but not longer than 3 years
- Diagnostic criteria as specified in the Int. Ass. for the Study of Pain (IASP) Classification of Chronic Pain
- Pain is due to a lesion of the PNS
- Neuropathic nature of the low back pain is confirmed by
  - A score >18 on the Pain Detect Questionnaire
  - Cutaneous and sensory testing confirms the involvement of dermatomes corresponding to L5-S1
- Test of muscle power, flexion, and reflexes support the diagnosis
- Imaging will be performed where necessary to confirm the diagnosis

Clinical

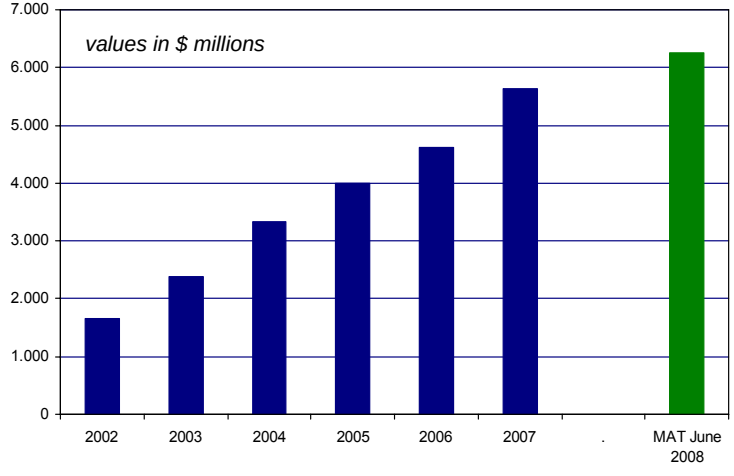
- Primary Efficacy Measure
  - Mean percent on 11-point Likert Scale measuring intensity of pain
- Key Secondary Measures
  - Mean percent change on the VAS (100mm line) measuring intensity of pain
  - Responder rate (30% and 50%) improvement on the Likert/VAS
- Safety Measures
  - ECG, Laboratory, Vital signs etc.

HF- 0220

Therapeutic intervention for neurodegenerative diseases

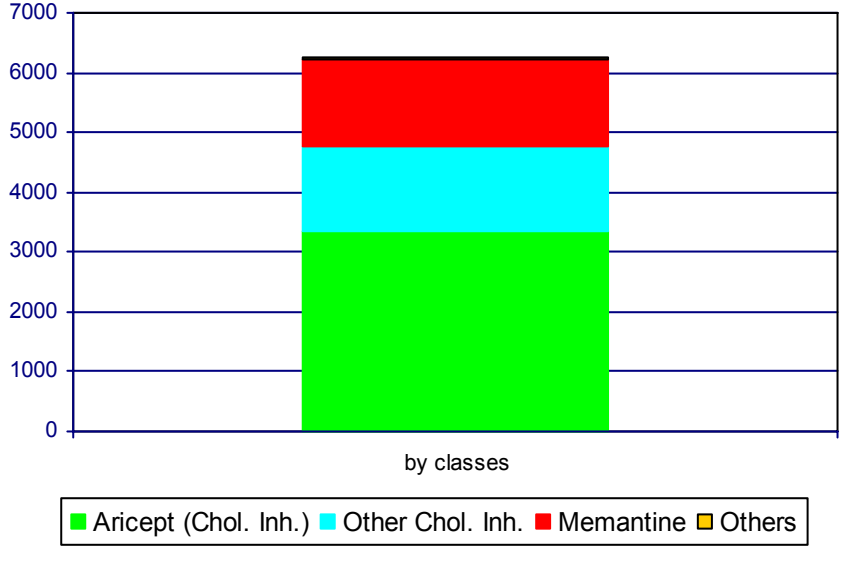


Alzheimer's disease drug market trend



Market growth of about 4 times since 2002

Market dominated by the cholinesterase inhibitors (donezepil - Eisai's Aricept; galantamine - J&J's Reminyl; rivastigmine - Novartis' Exelon) but the NMDA receptor antagonist memantine (Forest's Namenda and Lundbeck's Ebixa) ranks second on sales



Overall activity profile supports neuroprotective and anti-inflammatory potential of HF-0220

- Cytoprotection

In vitro: **from hypoxia, duroquinone, Aβ1-42 insults in neurons, from hypoxia/reperfusion in organotypic hippocampal slices from ischaemia in PC12 cells**

In vivo: **from Aβ25-35 insult, ischemia (4-VO, MCAO), AF64A neurotoxicity, reduction of neurotoxic fraction of Ab (soluble Aβ1-42) in transgenic mice**

In vitro: **myocardial infarction model in isolated heart**

- Neuronal Repair

In vitro: **induction of sensory and motor neuron neurite outgrowth protection of sensory neurons from cisplatin-induced damage**

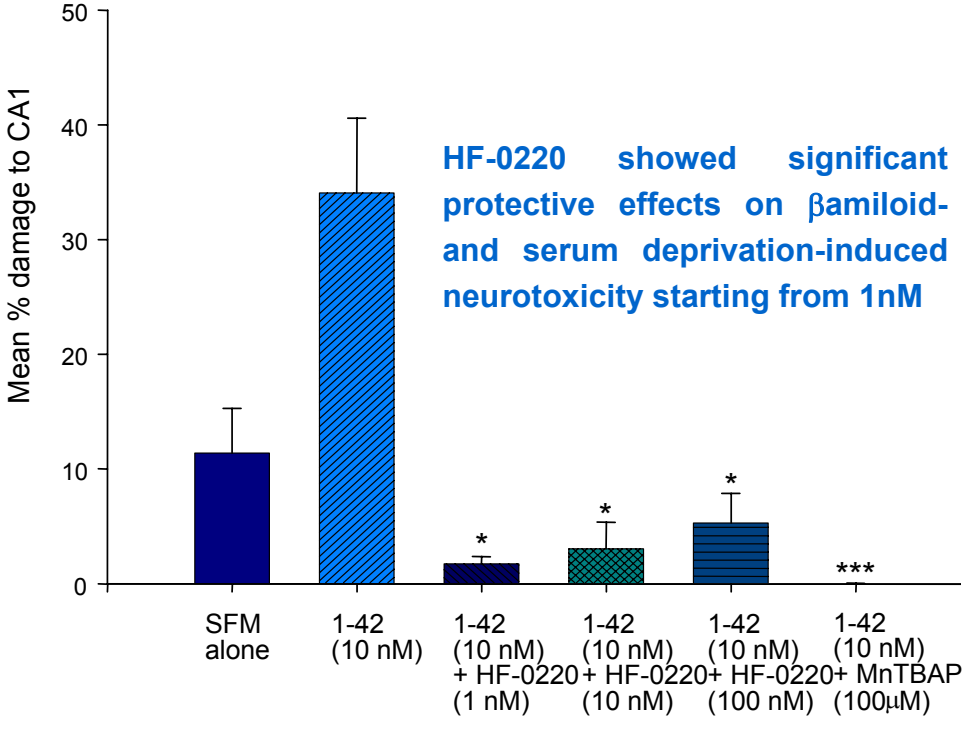
- Anti-inflammatory

In vitro: **increase of anti-inflammatory eicosanoid (15d-PGJ_2) and decrease of pro-inflammatory eicosanoids (PGE_2) in human PBMCs**

In vivo: **prophylactic effect in model IBD and RA model**

HF-0220 strongly protects organotypic hippocampal slices from neuronal damage

Aβ(1-42) + serum deprivation-induced neurotoxicity

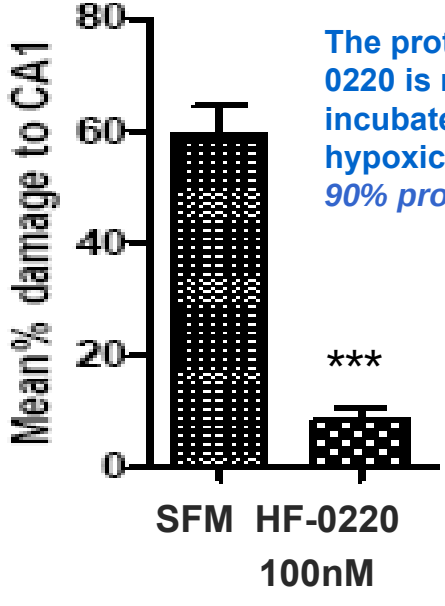


HF-0220 showed significant protective effects on βamiloid- and serum deprivation-induced neurotoxicity starting from 1nM

Organotypic hippocampal slice cultures were exposed to 10uM Aβ(1-42) and serum deprivation for 72h. Percentage of damage to hippocampal CA1 sub-region was scored 4 days later.

The free-radical scavenger MnTBAP was used as positive control.

hypoxia-induced neurotoxicity

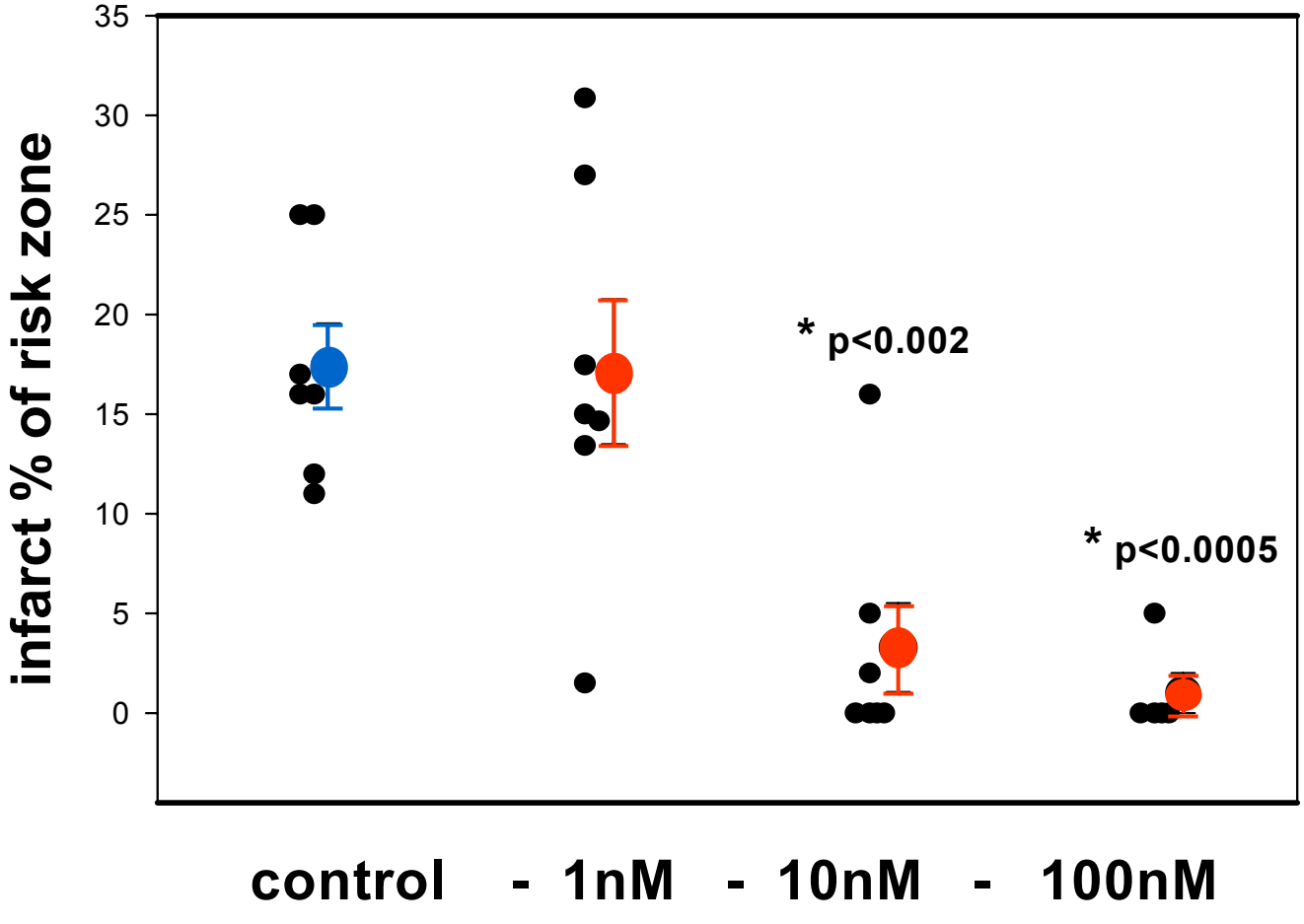


The protective effect of HF-0220 is maximal when pre-incubated 24h before the hypoxic stimulus (~ *90% protection)*

(Capsant Neurotechnologies,UK)

*Organotypic hippocampal slice cultures were exposed to 3hrs hypoxia (95%N_2/5% CO_2) followed by a 24 hrs of reperfusion. Compound was added to the cultures 24h prior to hypoxia. Neuronal damage was assessed as PI fluorescence in the CA1 sub-region. ***=p<0.001 vs hypoxia*

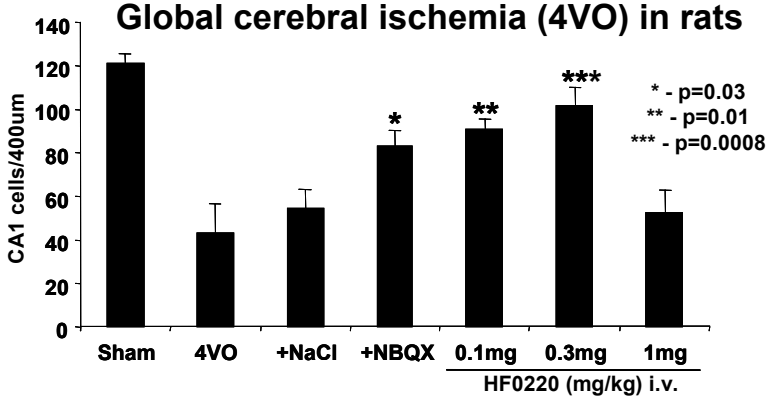
HF-0220 shows strong in vitro cardioprotective effects



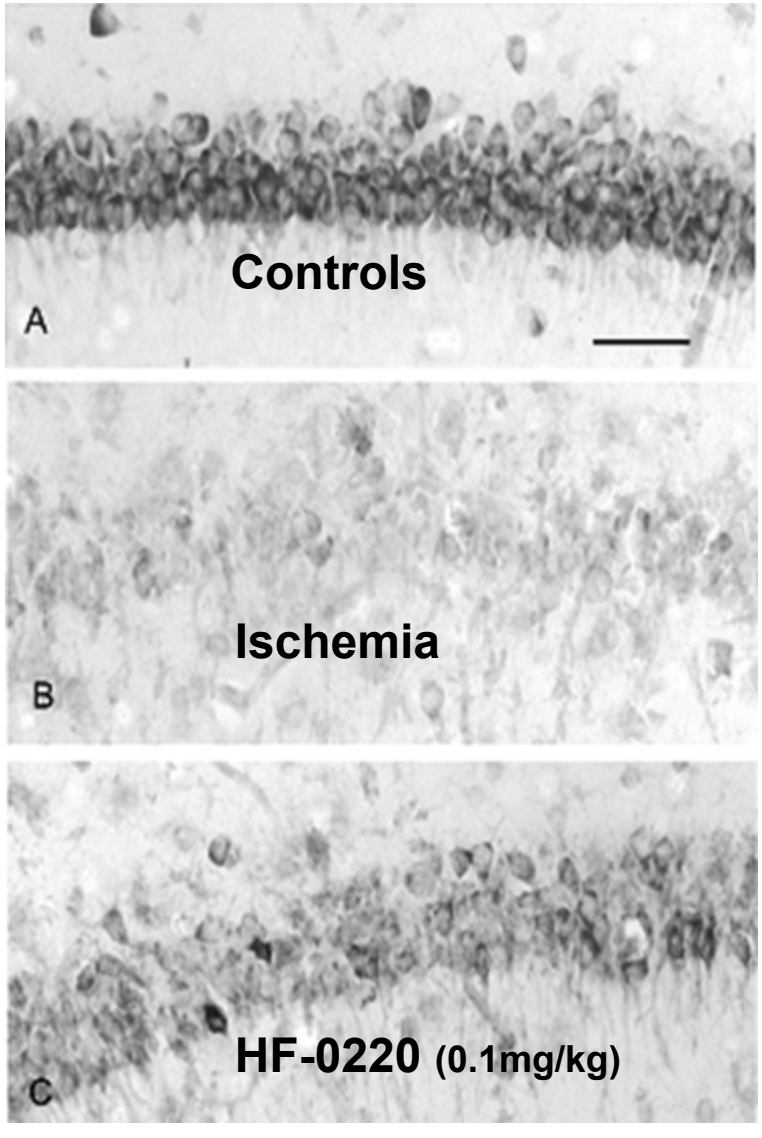
Protocol: 25min stabilisation, 30min exposure to vehicle or HF-0220,
5 min washout, 30min regional ischemia and 120min reperfusion

Kirsti Ytrehus
Dept of Medical Physiology
University of Tromsø

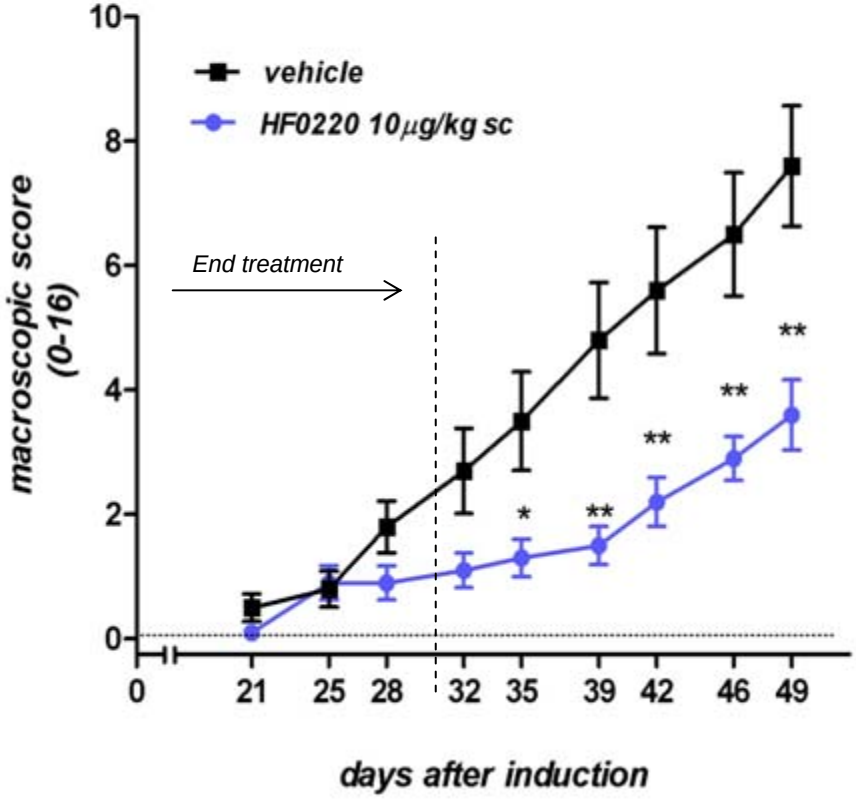
HF-0220 reverses global cerebral ischemia – induced cell loss



(FAN, Germany)

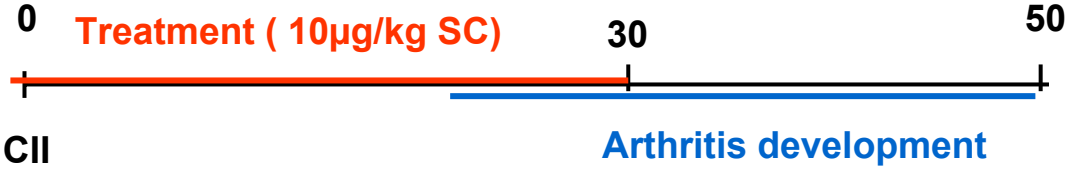


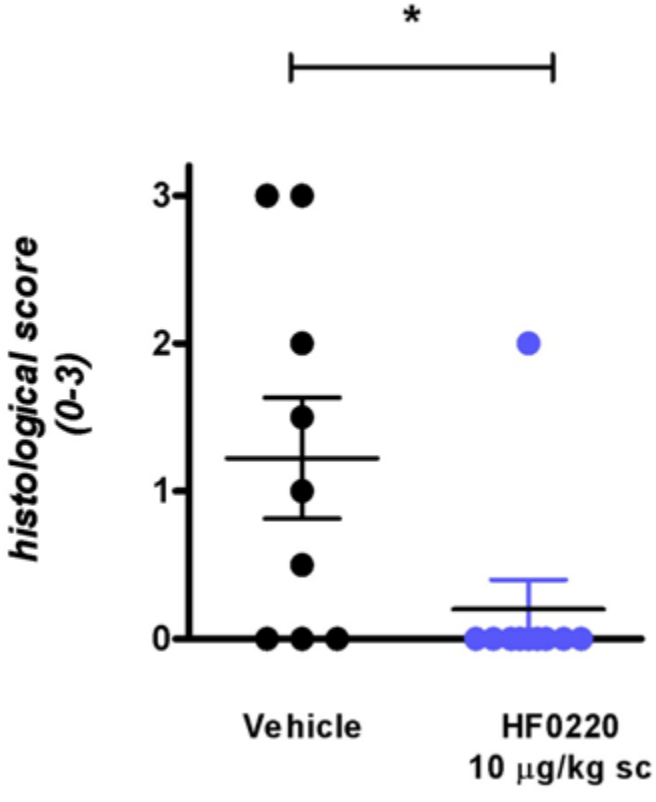
Protective effect of HF-0220 on murine CIA model of arthritis



Macroscopic score of arthritis

Protective effect of HF-0220 on murine CIA model of arthritis





Histology score ankle joints

The link between neurodegeneration and inflammation

Neuroinflammation represents one of the most dynamic areas in the search for new therapeutic targets for a spectrum of CNS diseases:

- In many chronic CNS disorders (e.g. AD, PD, vascular dementia) brain damage is associate with excessive microglia activation, with the release of inflammatory mediators and ROS formation, which are able to promote neuronal damage
- Dehydroepiandrosterone (DHEA) which is structurally similar to EPIA (of which in turn HF0220 is the 7-ß-hydroxyl derivative), is the most abundant steroid in human blood, and has a major role in the CNS where it increases neuronal excitability, has neuroprotectant property, and enhances memory in rodents. DHEA has been shown to display antioxidant properties
- As levels of DHEA decrease with age in humans, a causal link between falling DHEA levels and some age-related disorders such as ARCD, as well as AD has been proposed

HF-0220: conclusions from pharmacology

- HF-0220 showed strong neuroprotective effects in several experimental models of neurotoxicity
- HF-0220 modulated inflammatory response reducing pro-inflammatory and increasing anti-inflammatory mediators

Its unique mechanism of action makes HF-0220 a potential “first-in-class disease-modifying agent” for neurodegenerative diseases

Clinical Safety/Tolerability of HF-0220 in Patients with a Diagnosis of Mild to Moderate Alzheimer's Disease

Safety study design

- A multi-centre, multinational (UK, S, IN) randomised, double blind, placebo controlled study
- Two cohorts of patients
  - Multiple-dose escalating phase, dose ranging with dose increase every 7 days: 1-27mg/day (group 1) and 27-220mg/day (group 2)
  - Fixed dose phase: 1.5mg/day (group 1) and 15mg/day (group2) for 28 days

Safety study: key features

- Evaluate the Safety/Tolerability of HF-0220 in patient population.
- Evaluate feasibility of biochemical markers as surrogate end-points
- 42 male/female out-patients with AD aged above 55 years
  - Diagnosed in accordance with the NINCDS-ADRDA classification for probable AD
  - Mild/moderate AD dementia with MMSE score between 12 and 24

Safety study: key results

- Doses of 1 to 220mg/day well tolerated
- High completion rate overall
- Fixed dose phase 1.5 Vs 15mg/day Vs placebo
  - **Drop-out rate: nil**
  - **SAEs/ADOs/clinically notable AES: nil**
  - **AEs: no pattern of increased AEs compared with Pbo**
- Biomarkers: measurements made on plasma and CSF markers in subset of patients
  - **Confirm feasibility of performing these in subsequent trials**
  - **Sample size too small to assess any effect**

NW-3509

NW-3509 – innovative treatment for mania and other CNS diseases

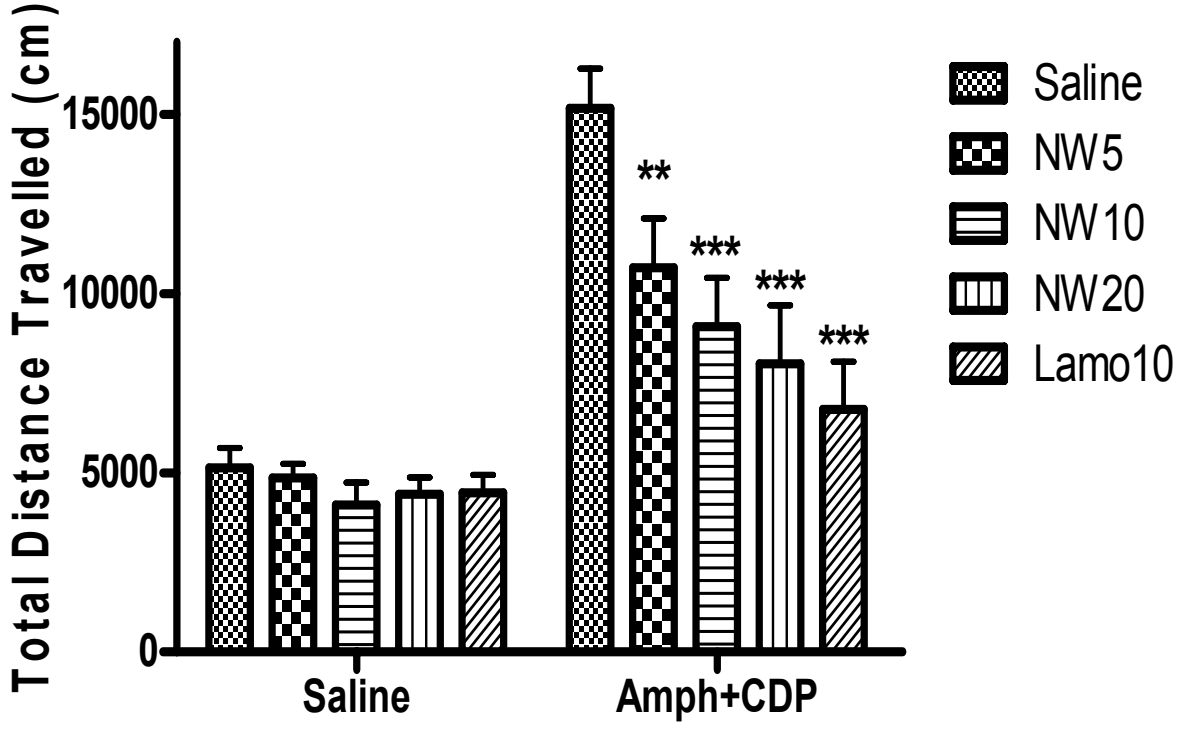
- Innovative compound from Newron's ion channel program
- Undergoing IND – enabling studies
- Potent and selective sodium channel blocker, acting on Nav 1.3, 1.7, 1.8
- Fast onset of action, high availability in the brain
- Modulating neuronal hyperexcitability, involved in several CNS indications
- Compound active in several models of CNS disease
- The compound is intended to be developed in bipolar disorder, cognitive impairment in schizophrenia, and other conditions that demonstrate impaired cognition
  - Severe medical conditions
  - High unmet medical need
  - Anti-psychotic drugs market value of more than $22bn with a growth of 11% in MAT Q2 2008

NW-3509 active in models relevant for different aspects of bipolar disorder and schizophrenia

- Manic hyperactivity phase
  - Amphetamine with Chlordiazepoxide induced hyperactivity
  - Sleep deprivation
- Depressive phase
  - Tail suspension test
- Information processing
  - PPI disrupted by different natural and pharmacological stimuli
- Cognitive impairment
  - Novel object recognition
- Obsessive compulsive behaviour
  - Marble burying test
- Aggressive behaviour
  - Resident intruder model

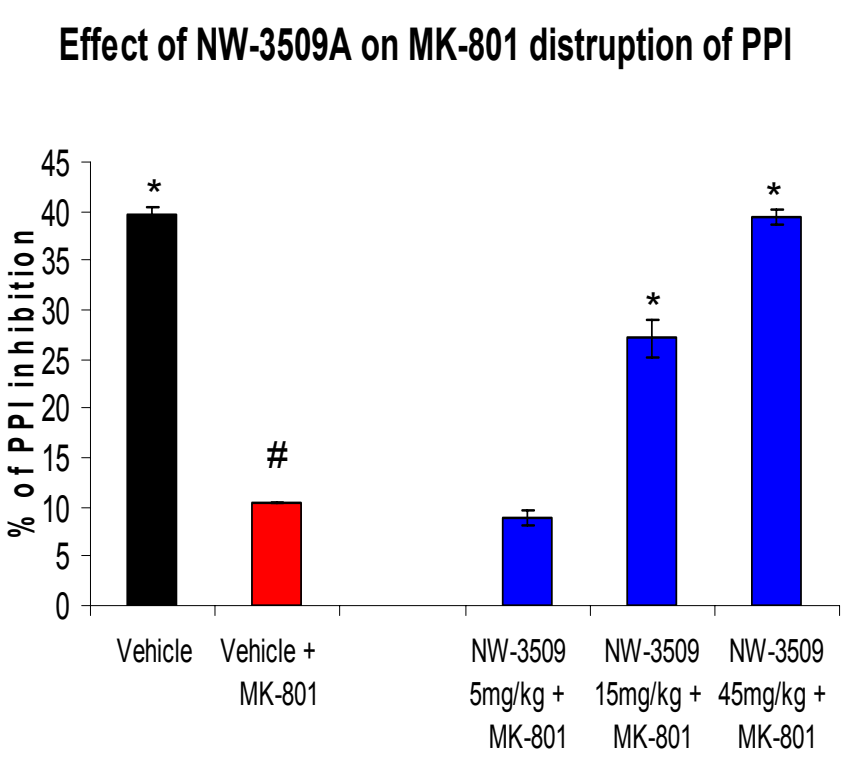
NW-3509 is active in a mania hyperactivity model in mice

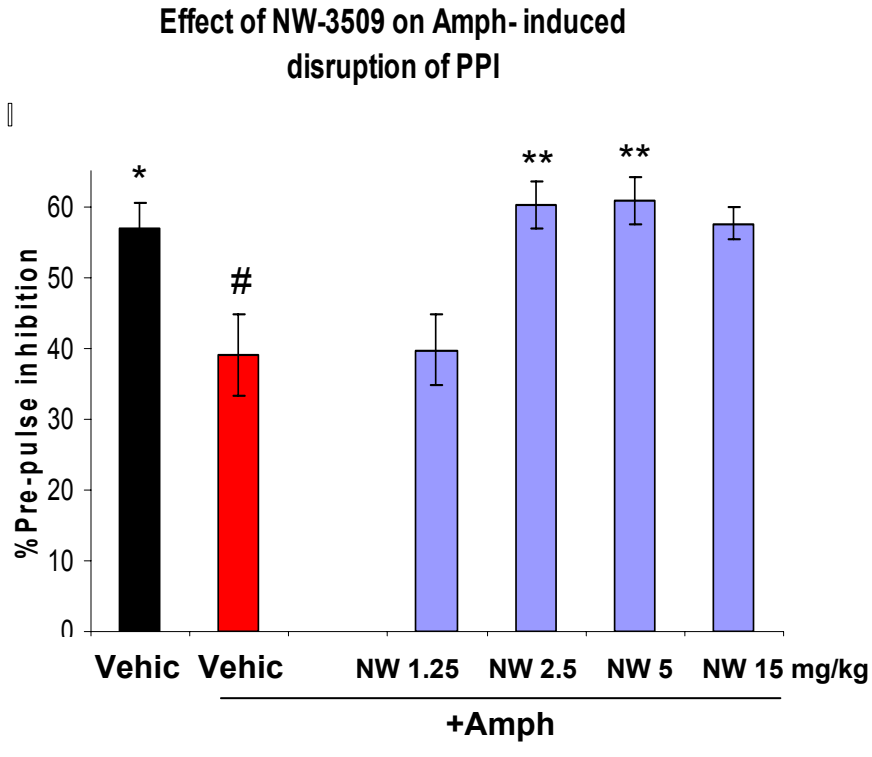
Amphetamine + Chlordiazepoxide hyperactivity model



Amph= amphetamine
CDP= Chlordiazepoxide

NW-3509 is active in the rat pre-pulse inhibition (PPI) disrupted by MK-801 and by Amph



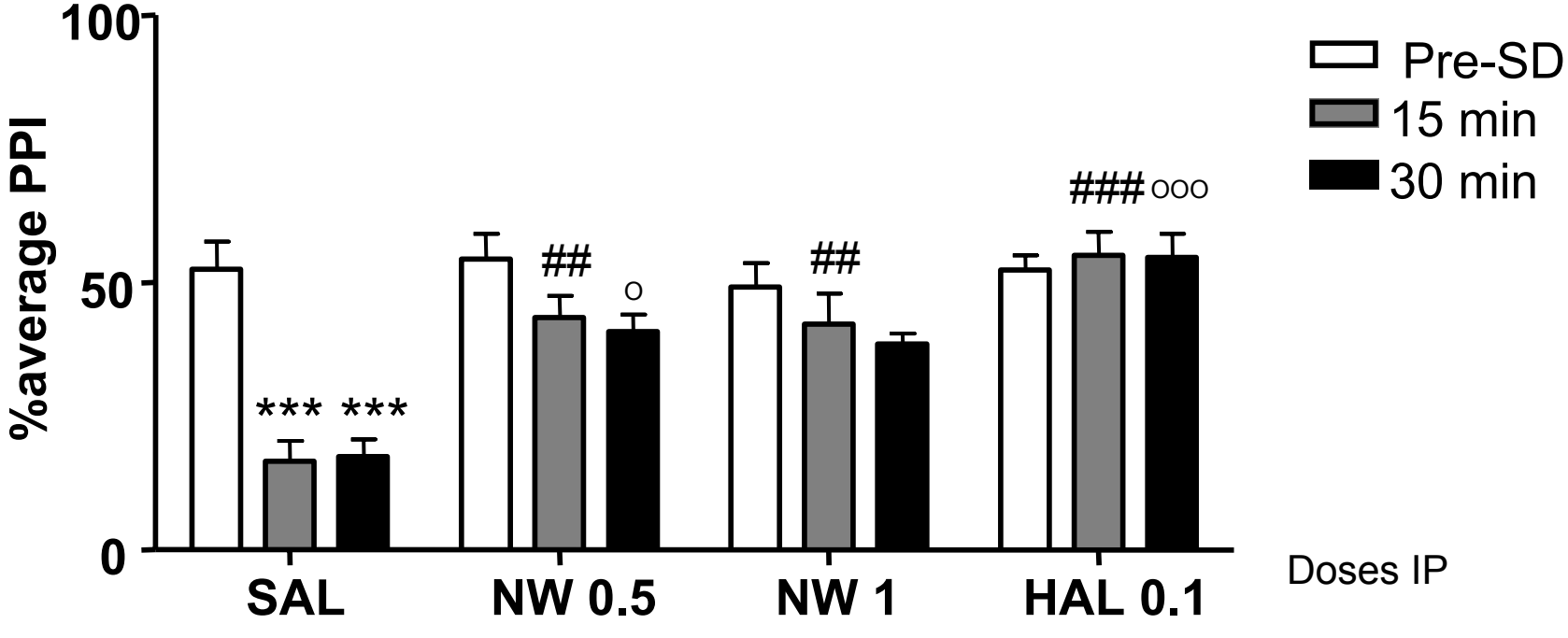


NW-3509 reverses MK801 and Amph-induced disruption of PPI at very low doses (range 2.5-15 mg/kg p.o.) without affecting basal locomotor activity

The PPI procedure is used to assess the subject's ability to "gate" or filter environmental information and provides operational measures of information processing that are abnormal in several neuropsychiatric disorders characterized by deficits in suppression or inhibition of intrusive or irrelevant stimuli.

NW-3509 is active in the rat pre-pulse inhibition (PPI) disrupted by sleep deprivation

Sleep deprivation (72hr) induces in rats hyperactivity and impairment of PPI, and is considered a natural model of mania

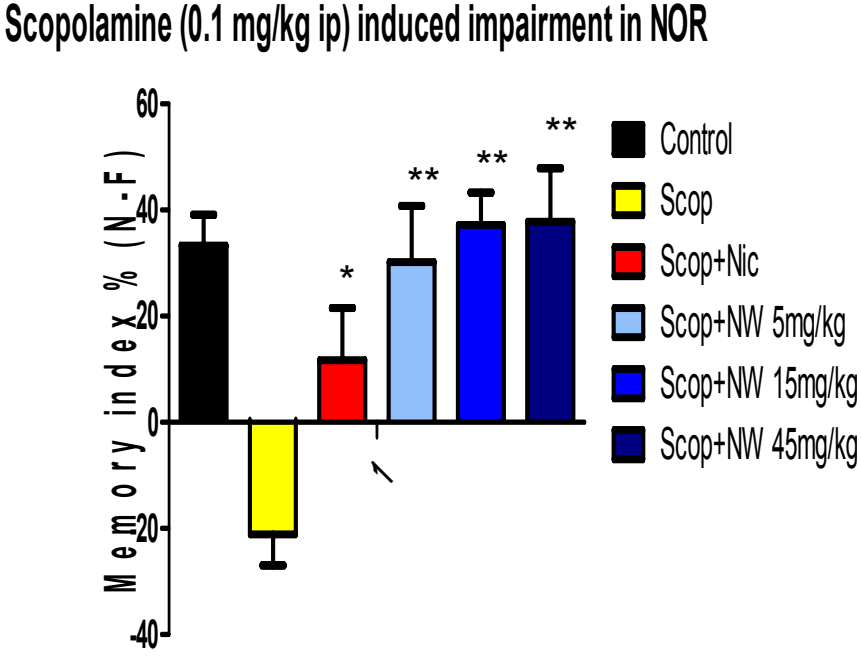


NW-3509 completely reverses SD-induced disruption of PPI at very low doses (range 0.5-1 mg/kg i.p.) without affecting basal locomotor activity

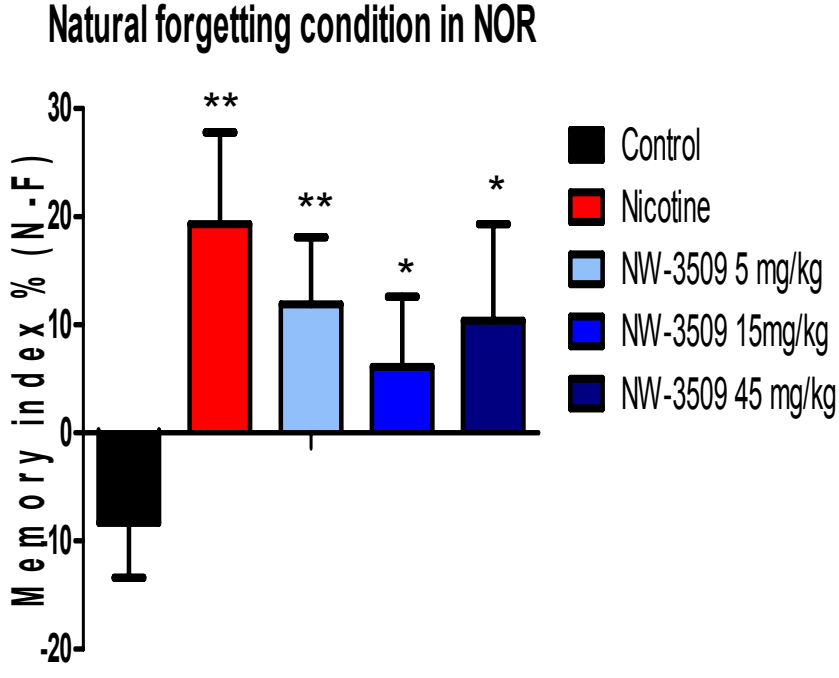
Effect of NW-3509 on PPI disruption induced by sleep deprivation. Data are expressed as mean±SEM of n=12 rats per group. %PPI was calculate over a 30 min and 15 min session. NW-3509 was administered 5 min before starting PPI test. ***, P<0.001 vs SAL PRE-SD ##; P<0.01 vs SAL 15 min; ###, P<0.001 vs SAL 30 min; o P<0.05 vs SAL 30 min; ooo P<0.001 vs SAL 30 min

NW-3509 reverses scopolamine and natural forgetting memory impairment in the NOR model

Effect on Short-term memory (ITI 1 hr)



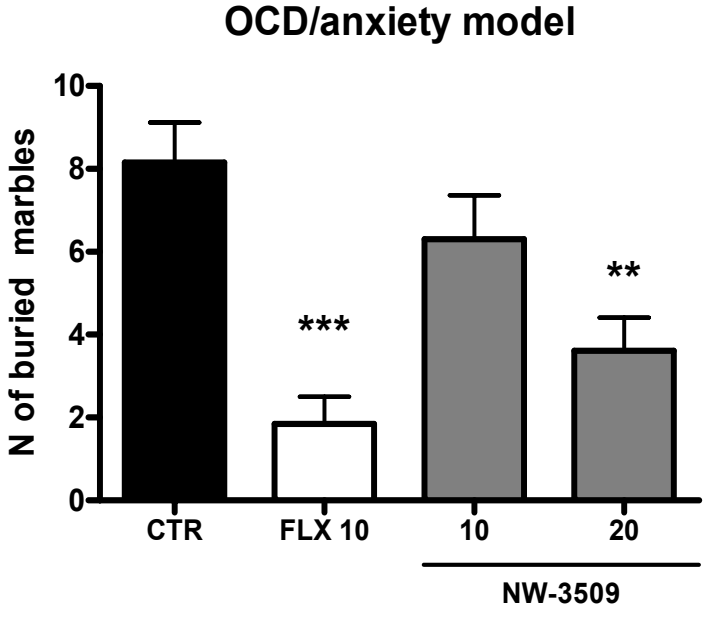
Effect on long-term memory (ITI 24hr)

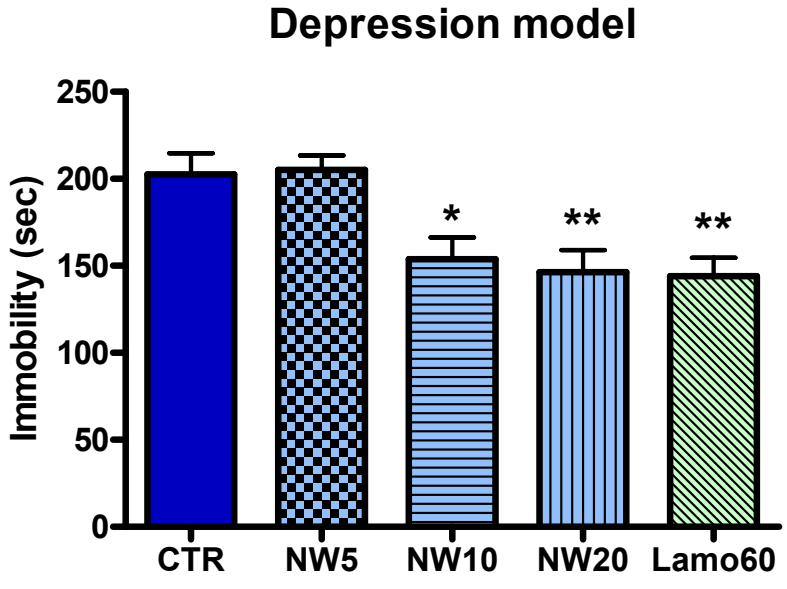


The effect of scopolamine was totally reduced and long-term memory was enhanced by NW-3509 at the all three doses tested (5, 10 and 45 mg/kg po)

The novel object recognition (NOR) task is a paradigm employed to detect both disruption and improvement of non-spatial memory in rats. Scopolamine impairment is usually reversed by several class of compound acting directly or indirectly on the cholinergic system.

OCD and depression: NW-3509 is active in the marble burying and tail suspension test





NW-3509 orally administered significantly decreased the number of marbles buried, fluoxetine (FLX) was used as positive standard

The Marble Burying Test (MBT) is considered an animal model of anxiety/obsessive-compulsive disorder (OCD). Mice which are placed individually in a cage containing a number of glass marbles spontaneously tend to bury the glass marbles present.

NW-3509 orally administered significantly decreased the immobility time (depression index) in the TST at lower doses than lamotrigine used as positive standard

The Tail Suspension Test (TST) is an animal model widely used and predictive of potential anti depressant drugs. Mice suspended by the tail after a while stop struggling and stay immobile. Immobility behavior is an index of depression/despair-like status

NW-3509: potential for treating several features of bipolar disorder and schizophrenia

- **NW-3509 is active in a hyperactivity mania model similarly to mood stabilizing drugs**
- **NW-3509 is active in the tail suspension test similarly to lamotrigine suggesting an effect also in the depressive phase of bipolar disorders**
- **NW-3509 is active in information processing model (PPI) disrupted by different mechanisms**
  - **This wide-ranging activity is a unique feature of NW-3509 since different class of mood stabilizers and antipsychotics are usually effective in one but not on the other pharmacological PPI impairment**
- **NW-3509 is active in short and long-term memory impairment**
  - **The ameliorative effect on cognition is an unexpected characteristic of this type of compounds since antipsychotics and mood stabilizers have usually no or detrimental effect on cognition**
  - **Cognitive impairment is often associated with psychiatric disorders representing an unmet medical need and NW-3509 has potential to improve this condition.**
- **NW-3509 is also active in the obsessive compulsive model strengthening its multifaceted activity**

Summary

- NW-3509 possesses a distinctive superior pharmacological profile versus current antipsychotics and mood stabilizer drugs
- Anti-mania, anti-depressive and anti-psychotic activity
- Strong activity against information processing and cognition impairment
- These pharmacological data support the therapeutic potential of NW-3509 particularly in cognitive impairment, an important unmet medical need of bipolar disorders and schizophrenia as many antipsychotics and mood stabilizer agents have detrimental effects on cognition

Financial review

Financial Highlights Half Year 2008

- First time consolidation of subsidiaries in CH and UK
- Gross R&D expenses €10.8m (net of MS reimbursement and R&D tax credit: €5.1m)
- SG&A expenses €5.3m including €1.3m one-time effect of HF post acquisition restructuring
- Financial income €1.1m
- Net loss €7.3m
- Cash balance €50.5m (incl. €2.9m in transfer)
- Guidance of full year cash burn of €25m confirmed

Anticipated 12 month milestones

- Top-line results safinamide as add-on to L-dopa in mid-to-late stage PD patients
- Start of additional studies to allow regulatory filing of safinamide in PD
- Start of Phase IIb/III study of ralfinamide in NLBP
- IND for NW-3509
- Start of PoC trial of HF-0220 as neuroprotectant

Summary Highlights

- Leading the field in the development of novel therapies for the treatment of CNS and pain
- Late stage validated pipeline addressing major therapeutic indications
- Broad, expanded pipeline:
  - 5 clinical stage compounds
  - 8 clinical indications
- Goal is to become a Fully Integrated Biopharmaceutical Company