



Addex Pharmaceuticals

ADX10059 Monotherapy Preliminary
Efficacy Data in GERD

16 November 2009



Disclaimer

These materials do not constitute or form part, or all, of any offer or invitation to sell or issue, neither in the United States of America nor elsewhere, or any solicitation of any offer to purchase or subscribe for, any securities, nor shall part, or all, of these materials or their distribution form the basis of, or be relied on in connection with, any contract or investment decision in relation to any securities.

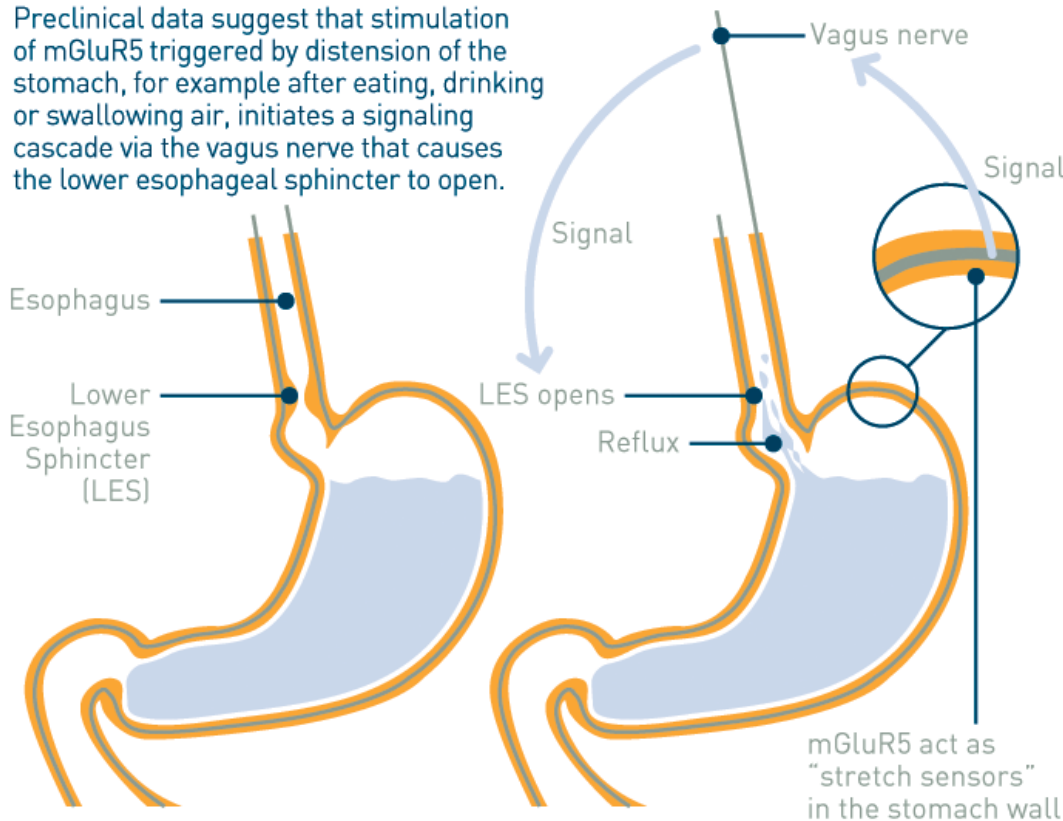
These materials contain forward-looking statements based on the currently held beliefs and assumptions of the management of Addex Pharmaceuticals Ltd, which are expressed in good faith and, in their opinion, reasonable. Forward-looking statements involve known and unknown risks, uncertainties and other factors, which may cause the actual results, financial condition, performance, or achievements of Addex Pharmaceuticals Ltd, or industry results, to differ materially from the results, financial condition, performance or achievements expressed or implied by such forward-looking statements. Given these risks, uncertainties and other factors, recipients of this document are cautioned not to place undue reliance on these forward-looking statements. Addex Pharmaceuticals Ltd disclaims any obligation to update these forward-looking statements to reflect future events or developments.

These materials are strictly confidential and must not be disclosed or distributed to third parties.

Why GERD with mGluR5 NAM?



Preclinical data suggest that stimulation of mGluR5 triggered by distension of the stomach, for example after eating, drinking or swallowing air, initiates a signaling cascade via the vagus nerve that causes the lower esophageal sphincter to open.



- Gastroesophageal Reflux Disease (GERD) is not caused by too much acidity
- GERD is caused by poor lower esophageal sphincter (LES) function
- mGluR5 in GERD
 - metabotropic glutamate receptor 5 (mGluR5)
 - found in stomach wall
 - triggered by “stretch sensors”
 - regulates LES function (via vagus nerve)
 - mGluR5 blockers normalize LES function in animals via peripheral mechanism¹
- ~15% of U.S. adults suffer from GERD
- ~\$25bn annual sales for anti-acids and anti-ulcerants
- ~40% of GERD patients not adequately treated by the indicated PPI dose²
- Only 50% of GERD patients satisfied with current treatment²
- Increasing PPI dose has not conclusively been shown to be effective - no PPI is licensed for twice-daily dosing

¹ *Am J Physiol Gastrointest Liver Physiol* 292: G501–G511, 2007

² *Gut* 2009;58:295–309

Ongoing Phase IIb GERD Monotherapy Study



Study [ADX10059-204](#)* (n = 90)

Started Dec '08

- ADX10059 MR monotherapy in patients with GERD, known to respond to PPIs
- Multi-center EU double-blind, placebo-controlled study of 120 mg twice-daily
- Two week symptom evaluation & baseline period
- Two week dose administration period
- Primary Outcome Measures
 - Number of GERD symptom free days (week 2 of study vs week 2 of baseline)
- Secondary Outcome Measures
 - GERD symptoms
 - Sleep disturbance
 - Use of antacid rescue medication
 - Global assessment of GERD
 - Effect on lower oesophageal sphincter and reflux episodes in a subset of patients
 - ✓ pH impedance (measures reflux)
 - ✓ manometry (measures sphincter function)

Reports Today!

* <http://bit.ly/qmq57>

Primary Endpoint *Symptom Free Days*



	Baseline	Treatment Week 2	% change	p value
ADX10059 120 mg bid	0.46	2.5	443%	0.0452
Placebo bid	0.72	1.71	138%	

LS Mean Treatment Difference at Week 2: 0.91 (p=0.0452)

Mechanistic Efficacy Endpoints Impedance



	Baseline week 2	Treatment week 2	% change	p value
All Reflux Events (mean)				
ADX10059 120 mg bid	64.9	47.9	-26%	0.0342
Placebo bid	77	78.4	+2%	
Acidic Reflux Events (mean)				
ADX10059 120 mg bid	52.1	37	-29%	0.0032
Placebo bid	55.7	59.7	+7%	

Major Secondary Endpoints



- Increased heartburn free days vs placebo ($p < 0.05$)
- Reduced sleep disturbance vs placebo ($p < 0.05$)
- Reduced use of antacid medication ($p < 0.05$)
- Reduced GERD symptoms (questionnaire) ($p < 0.05$)
- Patients preferred ADX10059 over placebo ($p < 0.05$)

Safety & Tolerability

ADX10059 120 mg bid (2 weeks)



- No significant changes in safety monitoring parameters
- Well tolerated
 - Some CNS side effects
 - majority mild
 - none severe
 - Tolerability profile suitable for GERD treatment

Ongoing Phase IIb PPI Add-On Study



Study [ADX10059-205](#)* (n = 280)

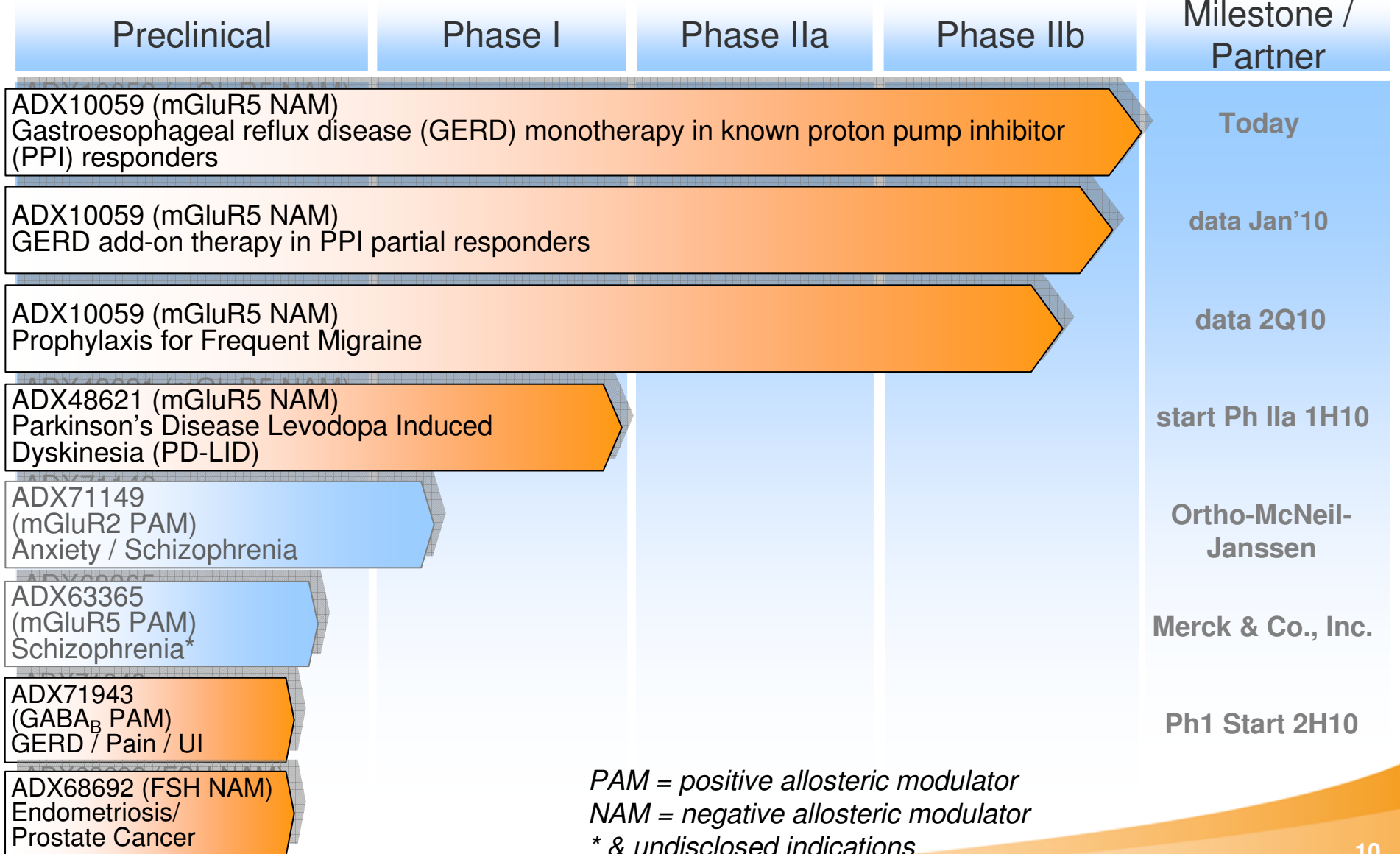
Started Dec' 08

- ADX10059 add-on therapy in GERD patients with partial PPI response
- U.S. & EU double-blind placebo-controlled, parallel group, dose range finding of twice-daily 50mg, 100mg or 150mg of ADX10059 MR
- Patients will continue on whichever PPI they were using prior to study
- One week baseline symptom evaluation period
- Four week administration period
- Primary Outcome Measures
 - Number of GERD symptom free days in week 4 of treatment vs baseline
- Secondary Outcome Measures:
 - GERD symptoms
 - Sleep disturbance
 - Use of antacid medications
 - Global assessment of GERD
 - Safety and tolerability assessments

Reports in Jan '10

* <http://bit.ly/Sy0Lt>

Allosteric Modulator Pipeline



PAM = positive allosteric modulator
 NAM = negative allosteric modulator
 * & undisclosed indications

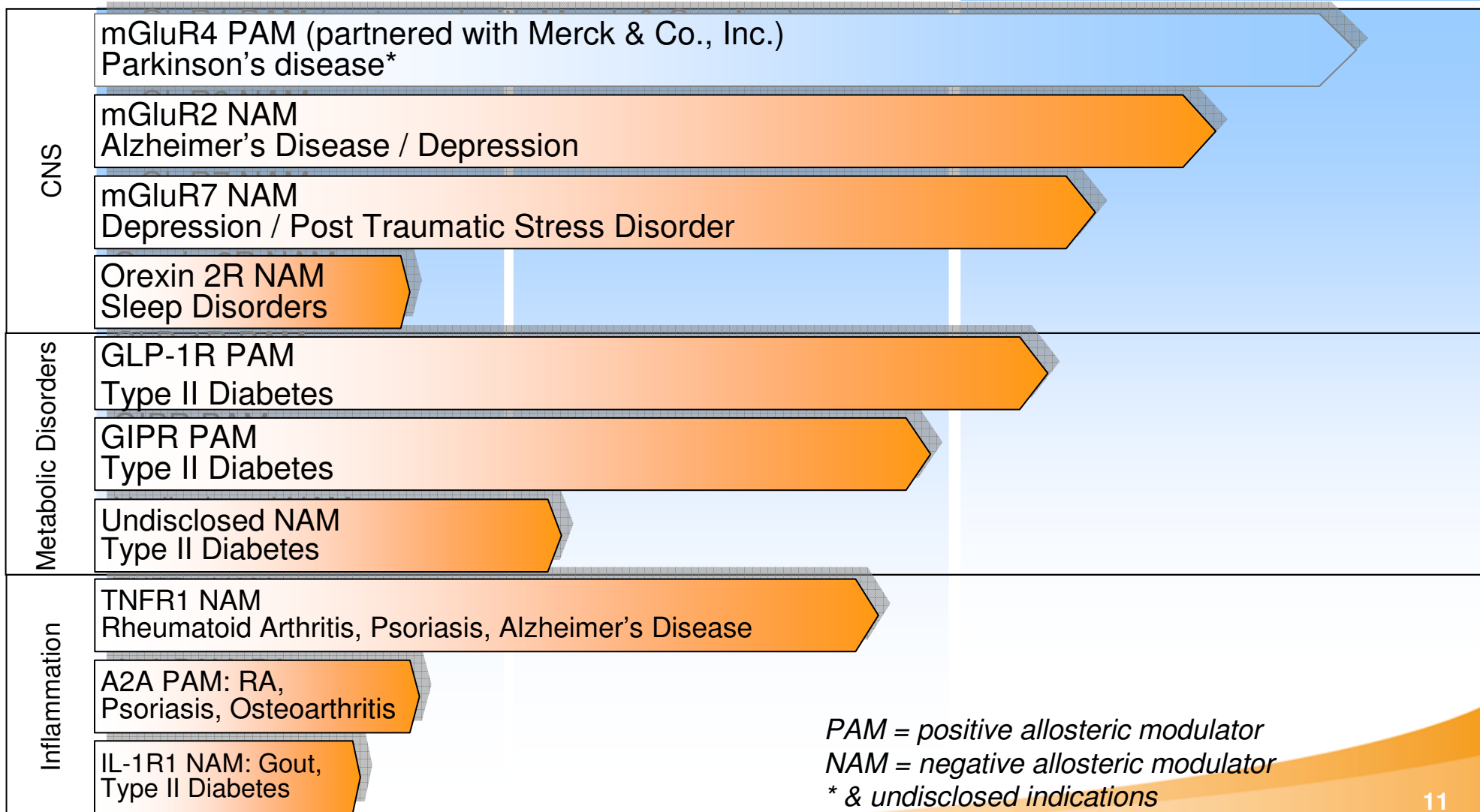
Allosteric Modulators in Discovery



Assay Dev & Screening

Hit-to-Lead

Lead Optimization



*PAM = positive allosteric modulator
 NAM = negative allosteric modulator
 * & undisclosed indications*

Q&A

allosteric modulators for human health

www.addexpharma.com