



Addex Pharmaceuticals

Investor Relations Presentation
March 2009



www.addexpharma.com



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The Company



- Addex is located in Geneva, Switzerland
- Goal: allosteric modulators for human health
- Focus: CNS, Inflammation, Metabolic Disorders
- 135 employees / founded in 2002
- Pipeline
 - 3 Phase IIb trials of ADX10059 ongoing in GERD & migraine
 - Phase I of ADX48621 complete; Phase IIa in PD-L1D starts 2H09
 - 12 preclinical programs
- Validating deals with Merck & Co. and Johnson & Johnson

Financials



- Cash at 31 Dec 2008: CHF119.5 m
- 2009 cash burn guidance: CHF40-45m
- Market cap (28 Feb 09): CHF188m (€126 / US\$161)
- SIX Swiss Exchange: ADXN (ISIN:CH0029850754)
- Five analysts set price targets from CHF34-70

Allosteric Modulator Pipeline



| Partner | Screening & Hit-to-Lead | Lead Optimization | Preclinical | Phase I | Phase IIa | Phase IIb | Milestone |
|-----------------------------------|--|-------------------|-------------|---------|-----------|-----------|------------------|
| | ADX10059 (mGluR5 NAM) monotherapy in PPI responders (study 204): Gastroesophageal Reflux Disease (GERD) | | | | | | Data 2H09 |
| | ADX10059 (mGluR5 NAM) add-on in PPI partial responders (study 205): Gastroesophageal Reflux Disease (GERD) | | | | | | Data 2H09 |
| | ADX10059 (mGluR5 NAM) prophylaxis for frequent migraine (study 206): Migraine Prevention | | | | | | Data 1H10 |
| | ADX48621 (mGluR5 NAM): Parkinson's Disease Levodopa Induced Dyskinesia (PD-LID) | | | | | | PhIIa start 2H09 |
| Merck & Co., Inc. | ADX63365 (mGluR5 PAM): Schizophrenia* | | | | | | |
| Ortho McNeil Pharmaceutical (J&J) | ADX71149 (mGluR2 PAM): Anxiety / Schizophrenia | | | | | | |
| | ADX71943 (GABAB PAM): Pain / UI / GERD | | | | | | |
| | ADX68692 (FSH NAM): Contraception / Osteoporosis | | | | | | |
| | Adenosine A3 Antagonist : Glaucoma | | | | | | |

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

Allosteric Modulators in Discovery

| Partner | Hit-to-Lead | Lead Optimization |
|-------------------|---|-------------------|
| Merck & Co., Inc. | mGluR4 PAM: Parkinson's Disease* | |
| | GLP1R PAM: Type II Diabetes | |
| | mGluR7 NAM: Depression / Post Traumatic Stress Disorder | |
| | mGluR2 NAM: Alzheimer's Disease / Depression | |
| | Type II Diabetes | |
| | Obesity | |
| | Migraine | |

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

Deal Summaries



| Partner | Product | Indication(s) | Status at signing | Upfront Cash | Additional Milestones |
|---|------------------------|-------------------------|--------------------|----------------------------|-----------------------|
| Ortho McNeil Pharmaceutical Inc. (a J&J company) | ADX71149 mGluR2 PAM | Anxiety & schizophrenia | Hit-to-Lead | €3 million* (Dec 2004) | Not disclosed |
| Merck & Co., Inc. | mGluR4 PAM | Parkinson's disease** | Hit-to-Lead | \$3 million (Dec 2007) | \$167.5 million |
| Merck & Co., Inc. | ADX63365 mGluR5 PAM | Schizophrenia** | Clinical Candidate | \$22 million (Jan 2008) | \$680 million |

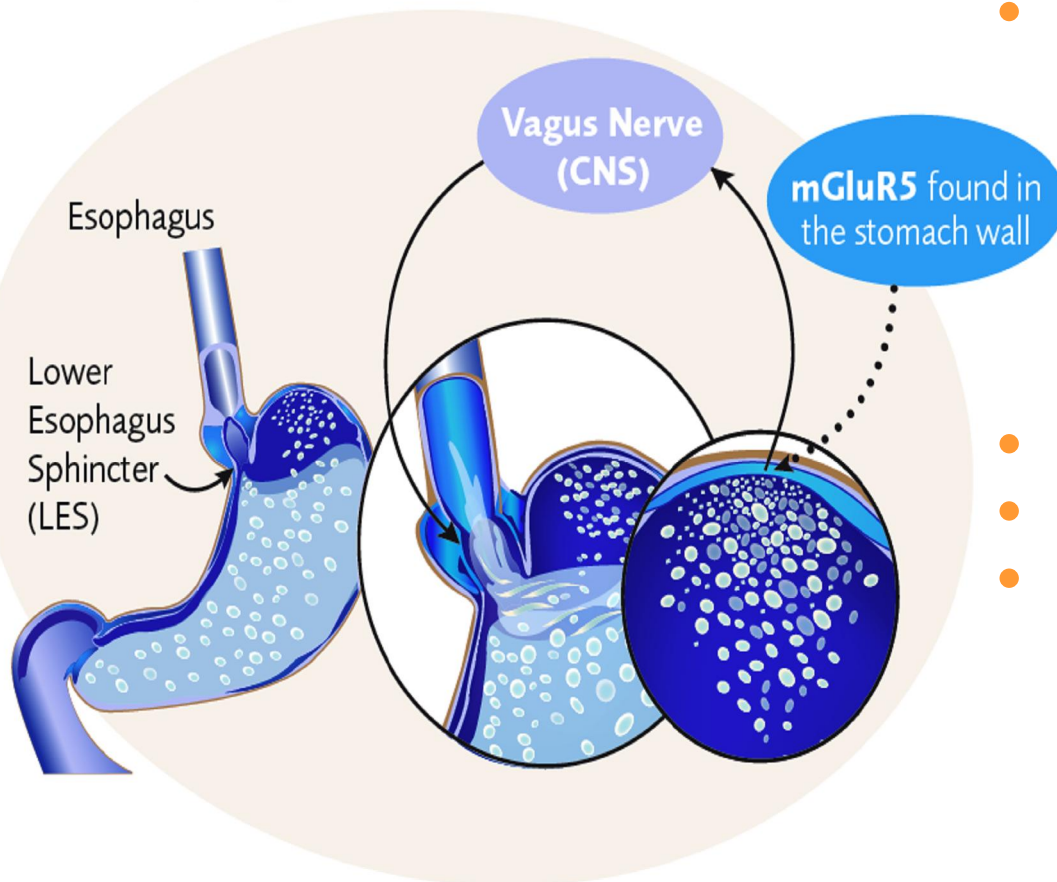
* research funding received from J&J: €4.2 million

** & other undisclosed indications

ADX10059 in GERD (Gastroesophageal Reflux Disease)



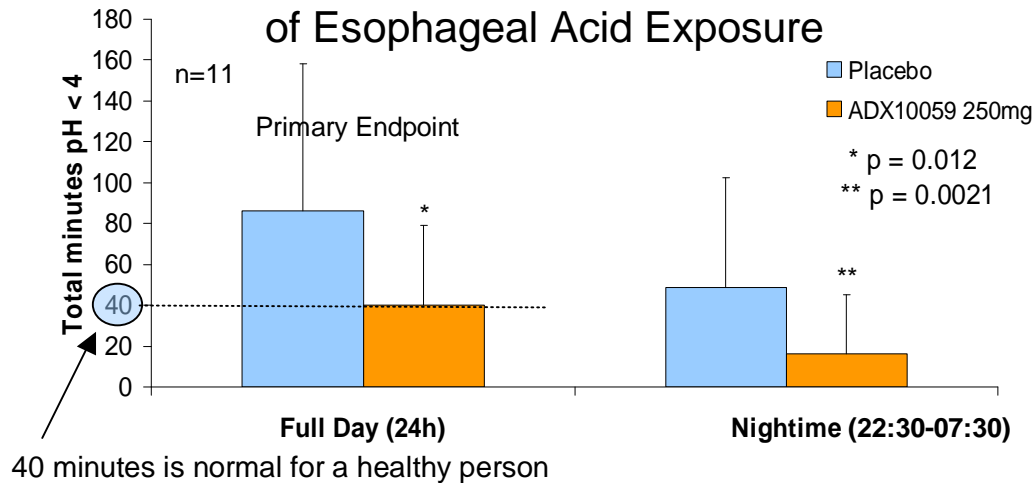
- GERD is not caused by too much acidity
- GERD is due to poor lower esophageal sphincter (LES) function
- mGluR5 in GERD
 - metabotropic glutamate receptor 5 (mGluR5)
 - Ø found in stomach wall
 - Ø Act as “stretch sensors”
 - Ø regulate, via vagus nerve, LES function
 - mGluR5 blockers normalize LES function in animals
- ~15% of U.S. adults suffer from GERD
- ~\$25bn market for anti-acids and anti-ulcerants
- Leading treatments
 - Have no effect on LES function
 - Up to 50% not adequately controlled by PPIs
 - Nocturnal GERD represents an unmet need



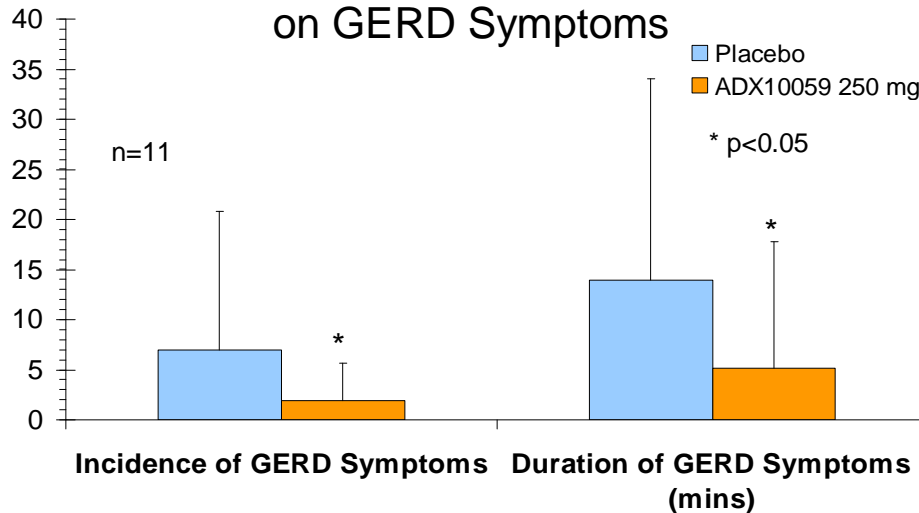
Review: ADX10059 Ph IIa Clinical Proof of Concept in GERD



Mean Total Duration of Esophageal Acid Exposure



Patient Reported Efficacy on GERD Symptoms



DESIGN

- Single-blind Phase IIa trial in 24 GERD patients
 - PPI responders not taking PPIs
 - Placebo tid on day 1
 - ADX10059 50mg or 250 mg tid on day 2
- Primary endpoint: Esophageal acidity
 - % time pH<4 /24h
 - measured using pH sensor in lower esophagus
 - drop in pH is a surrogate measure of reflux
- Secondary endpoints:
 - nighttime pH monitoring,
 - Post-prandial & other pH monitoring parameters
 - patient reported clinical symptoms

DATA

- Primary & secondary endpoints met
- All safety monitoring parameters normal
- Majority experienced CNS side effects
 - dizziness, drunk feeling, flushing
 - probable cause: rapid absorption of API

CONCLUSION: Develop modified release (MR) formulation to slow absorption of API

Study ADX10059-104

Part One Design



Part One (n = 12)

Design: single-dose, three-way crossover comparing

- 250mg API in capsules
- 250 mg ADX10059 MR1
- 250 mg ADX10059 MR2

Objectives:

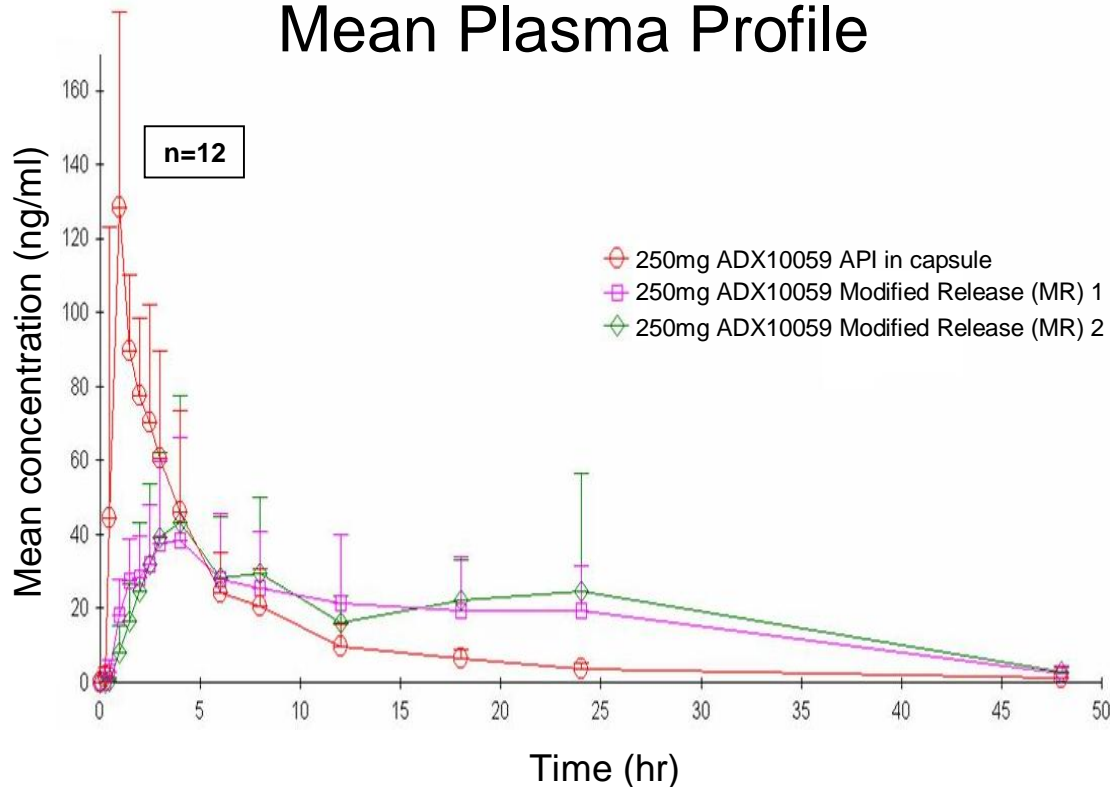
- compare pharmacokinetics (e.g. rate of absorption)
- compare safety and tolerability

Study ADX10059-104

Part One Results



Mean Plasma Profile



- Pharmacokinetics observed:
 - MR reduced rate of absorption compared to API in capsule
 - MR reduced time to Cmax compared to API in capsule
 - no change in 24 hour exposure for MR vs API in capsule
- PK after single dose suggested MR suitable for twice daily dosing
- AE profile markedly improved with MR formulations:
 - no dizziness, drunk feeling, or flushing in patients receiving MR
 - Seven of 12 patients receiving original API experienced expected effects
- All safety monitoring parameters normal
- ADX10059 MR1 was selected for Part Two of Study 104

Study ADX10059-104 Part Two Design



Part Two (n = 24)

- Design: ADX10059 MR1 six days with multiple ascending doses
 - 3 cohorts of 8 healthy volunteers received treatment for 6 days
 - » 6 subjects in each cohort receive ADX10059 MR1 (50mg, 125mg or 250mg) twice daily
 - » 2 subjects in each cohort receive placebo twice daily
 - Reflux provocation test with impedance pH monitoring on
 - » (pre-treatment) Day -1
 - » treatment Day 6
- Primary Objective
 - Pharmacokinetics of repeat dosing
 - Safety and tolerability of repeat dosing
- Secondary Objective
 - pharmacodynamic evaluation in GERD model
 - identify doses for Phase IIb

Study ADX10059-104 Part Two

Pharmacodynamic Data



- Dose-dependent treatment effects vs placebo after reflux provocation test
 - on the percentage of total acid exposure ($p = 0.0483$)
 - on the post-prandial number of weakly acid reflux episodes ($p = 0.0411$)
- Significant effects ($p < 0.05$) seen for the ADX10059 125 mg vs placebo and 250 mg doses vs placebo in multiple individual key parameters, including:
 - impedance measured reflux
 - weakly acidic reflux
 - acid exposure percent
 - bolus exposure percent
- No efficacy advantage for 250mg vs 125mg
- Trends achieved with the 50mg dose group
- Dramatic reduction in CNS side effects compared to API in capsule

Study ADX10059-105

food/PPI interaction



Design (n=15)

- A three-way crossover:
 - modified release ADX10059 250mg (single dose)
 - food
 - esomeprazole (Nexium)
- Objective: pharmacokinetics, safety & tolerability

Results

- Absorption of modified release ADX10059 not affected by food or esomeprazole
- Safety and tolerability suitable for chronic testing

Phase IIb GERD Monotherapy



Study ADX10059-204 (n = 90)

Started Dec '08

- ADX10059 MR **120mg twice-daily** in patients with GERD, known to respond to PPIs but not on acid suppressant therapy
- European multi-center, double-blind, placebo-controlled study
 - Two week baseline symptom evaluation period followed by two weeks dose administration
 - Objectives:
 - patient reported symptom control compared to baseline
 - manometry in patient subset (measure of esophageal function)
 - pH impedance in same patient subset (measure of acid reflux)
 - safety & tolerability

Reports in 2H09

Phase IIb PPI Add-On Study



Study ADX10059-205 (n = 280)

Started Dec' 08

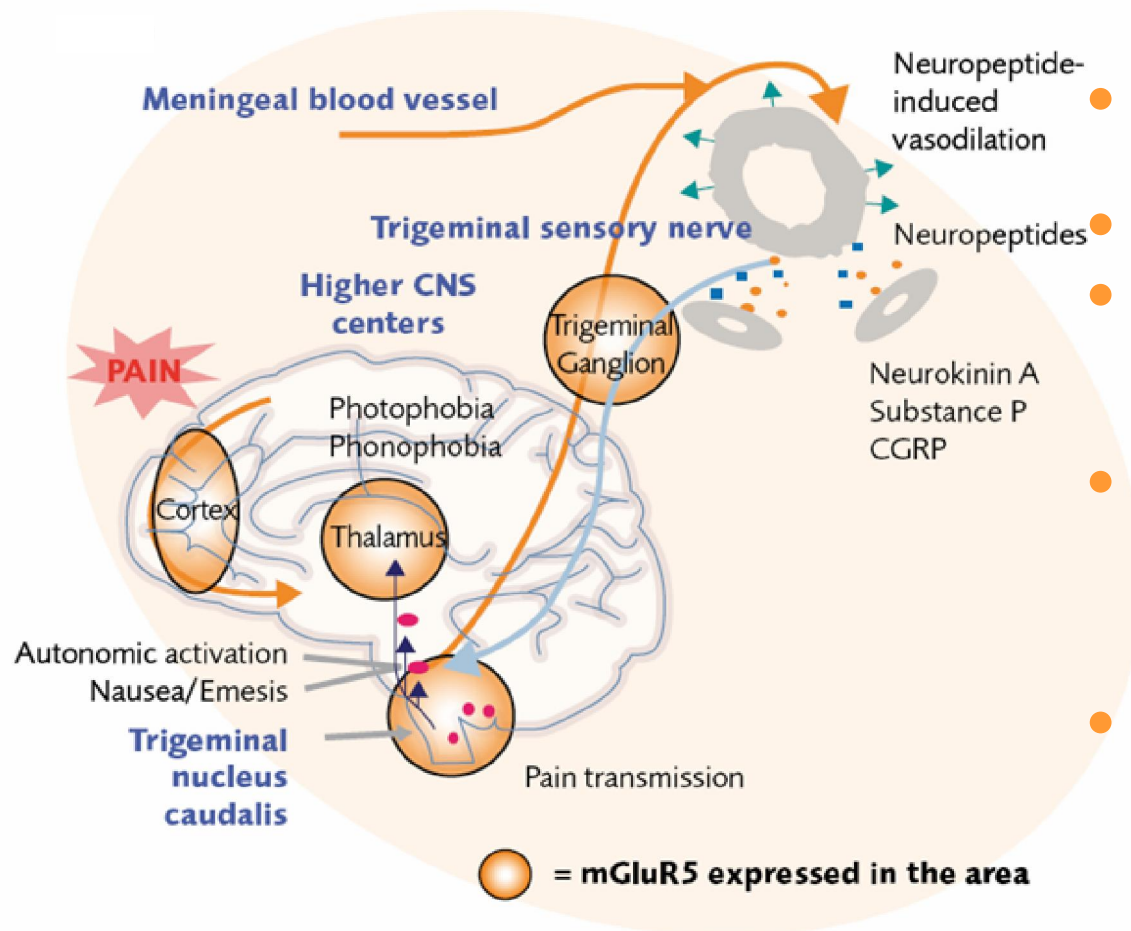
- ADX10059 add-on therapy in GERD patients with partial PPI response
- U.S. & EU double-blind placebo-controlled, parallel group, dose range finding of twice-daily 50mg, 100mg or 150mg of ADX10059 MR
- Patients will continue on whichever PPI they were using prior to study
 - none of the PPIs are excluded
 - histamine H2 antagonists & other antacids are excluded
- Two week baseline symptom evaluation period (with uninterrupted continuation of PPI use) followed by four week administration period
- Objectives:
 - patient reported symptom control (treatment vs baseline)
 - safety and tolerability

Reports in 2H09

mGluR5 for Migraine Prevention



mGluR5 is found throughout the Migraine Circuit



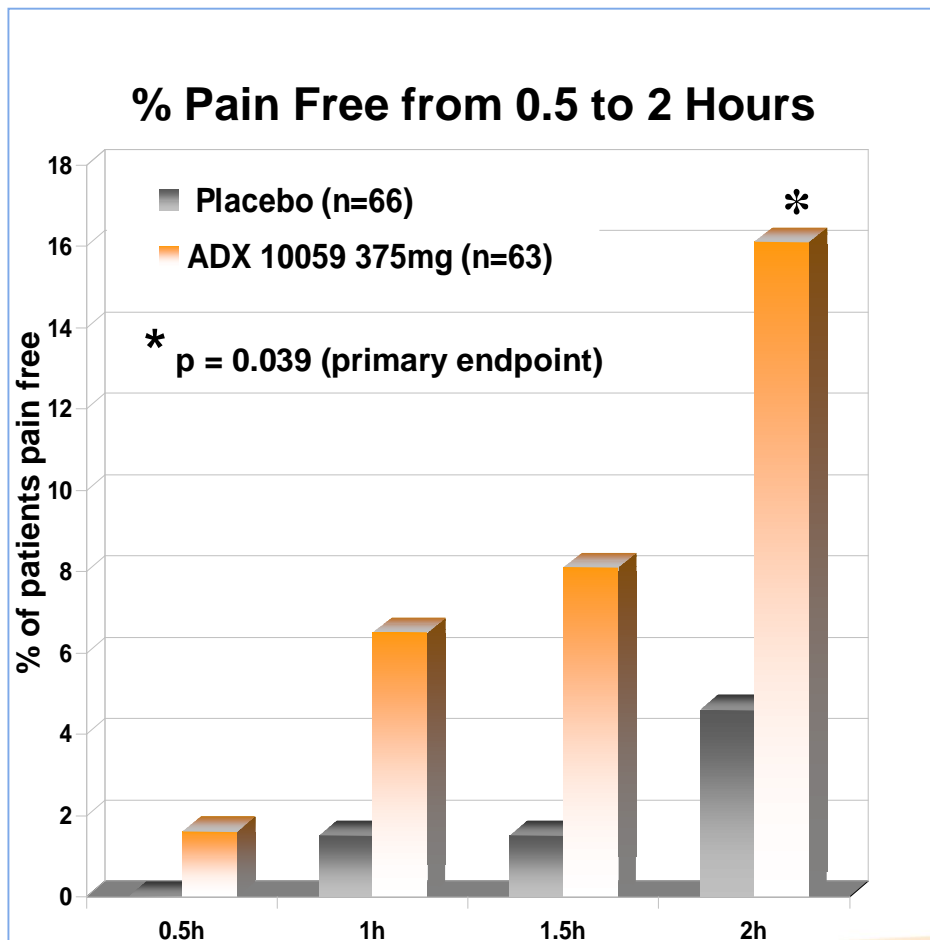
- The “migraine circuit” is a positive feedback loop leading to inflammation, pain, etc.
- Glutamate mediates relays in migraine circuit
- mGluR5 is in migraine circuit brain regions
- 12% prevalence (~30 million U.S. patients)
 - ~25% of migraineurs have 3+ attacks/month
 - avoiding migraines is better than treating them
- 2007 Topamax sales : \$2.4 billion (primarily for migraine prevention and epilepsy)
 - 15% of migraineurs use prophylactic drugs
 - Topamax goes off patent in 2009
- Triptans are not appropriate for prevention because they treat symptoms

ADX10059 Efficacy in Acute Migraine



Study 201 Design

- Double-blind, placebo-controlled, U.K. & German Phase IIa study in 129 patients
- Primary endpoint: IHS Grade 0 (pain free) at 2 hrs



Findings

- First time mGluR5 modulation shown to have efficacy in migraine
- Statistically significant efficacy on pain free endpoint in acute migraine is a high hurdle for a neural mechanism
- Evidence of effect starts 1 hour after dosing

Conclusions

- mGluR5 is involved in migraine circuit
- Acute effect, tolerability and neural mechanism all support development for prevention

Next for ADX10059: Phase IIb Migraine Prevention Trial



Study ADX10059-206 (n = 300)

Started Dec' 08

- Dose ranging (25mg, 50mg or 100mg of ADX10059 MR)
 - once daily administration during treatment weeks 1 & 2
 - twice daily administration during treatment weeks 3-12
- European multi-center, double-blind, placebo-controlled, parallel group study
 - patients with at least 3 attacks per month
 - patients diagnosed with migraine according to IHS criteria
 - 4 week baseline evaluation period
 - 12 week treatment period
- Outcome measures: migraine frequency and severity (treatment period vs baseline)

Reports in 1H10

mGluR5 NAM for levodopa induced dyskinesia



- Ph II Clinical validation of AFQ056 mGluR5 NAM by Novartis
 - Ü alleviated PD levodopa induced dyskinesia (LID) in
 - Ü alleviated PD symptoms in Ph II
- mGluR5 NAM alleviates PD-LID in primates
 - Ü AFQ056 increased efficacy of levodopa
 - Ü mGluR5 NAM potential levodopa sparing strategy (holy grail for PD)
- PD-LID is relatively straightforward development
 - Trials are shorter and easier for PD-LID than for PD
 - Endpoints are clear (UPDRS movement rating scale)
 - Addex can pursue into Ph II or III
- PD-LID product may receive FDA Fast Track status

Clinical Milestones



| Product | Trial | Objectives | When |
|----------|-----------|---|----------------------|
| ADX10059 | Phase IIb | GERD symptom control as monotherapy (study ADX10059-204) | data 2H09 |
| ADX10059 | Phase IIb | GERD symptom control as an add-on to PPIs (study ADX10059-205) | data 2H09 |
| ADX10059 | Phase IIb | reduce migraine frequency and severity (study ADX10059-206) | data 1H10 |
| ADX48621 | Phase IIa | Parkinson's disease levodopa induced dyskinesia (PD-LID) | start 2H09 |
| ADX63365 | Phase I | PK/tolerability (schizophrenia) | ND (Merck & Co.) |
| ADX71149 | Phase I | PK/tolerability (anxiety/schizophrenia) | ND (J&J) |
| ADX71943 | Phase I | PK/tolerability (UI/Pain/GERD) | start 4Q09 / 1Q10 |

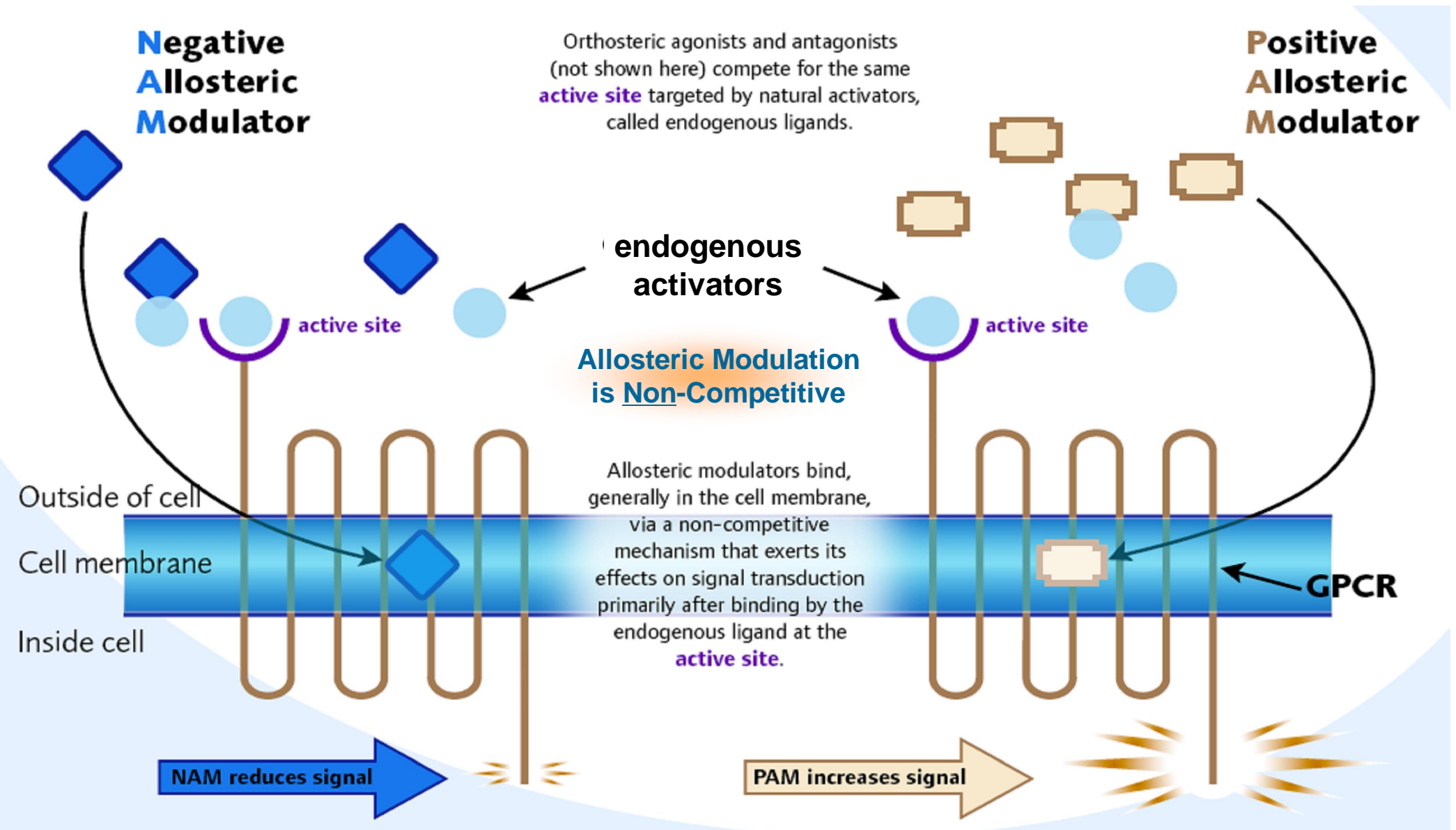
Allosteric Modulation Explained

Necessity is the Mother of Invention



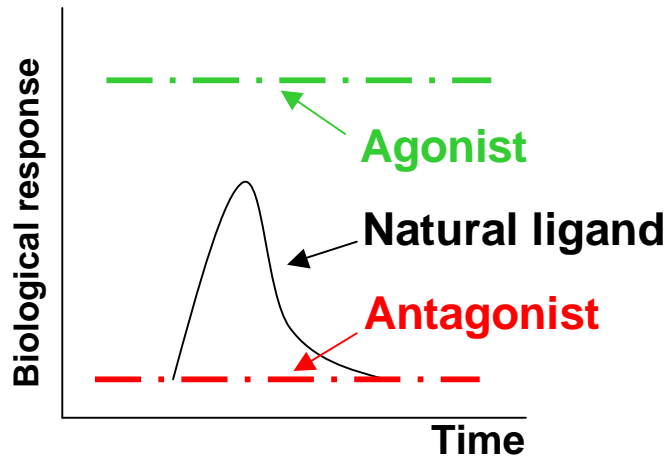
- Glutamate is *the* major neurotransmitter
- Even after 30 years, most attempts to drug glutamate receptors fail
- Knowledge about the functioning of mGluR₁₋₈ has been accumulated
- To drug mGluRs Addex pioneered tools for allosteric modulator discovery
 - Addex has built a proprietary allosteric modulator focused library (70k compounds & growing)
 - Addex has built screening tools capable of direct detection of allosteric modulators (facilitating discovery and medicinal chemistry)
 - Allosteric modulators have broad potential for GPCRs & potentially other receptors, including peptide receptors

Allosteric Modulation Explained

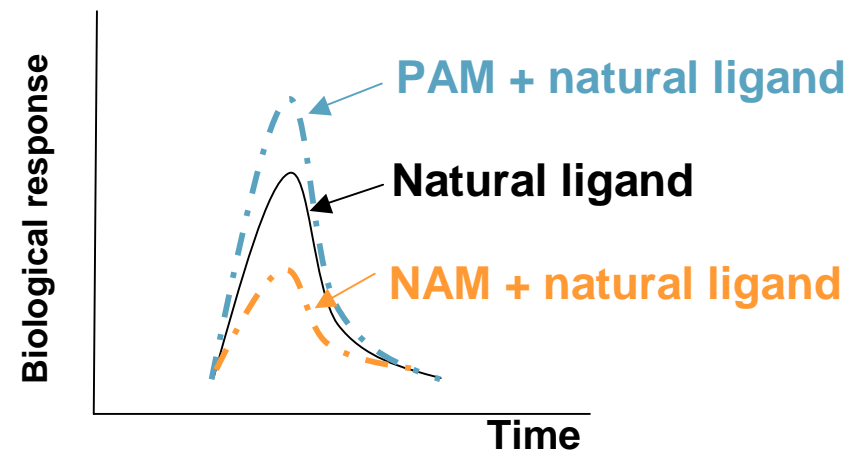


Orthosteric \neq Allosteric

Orthosterics are steady state

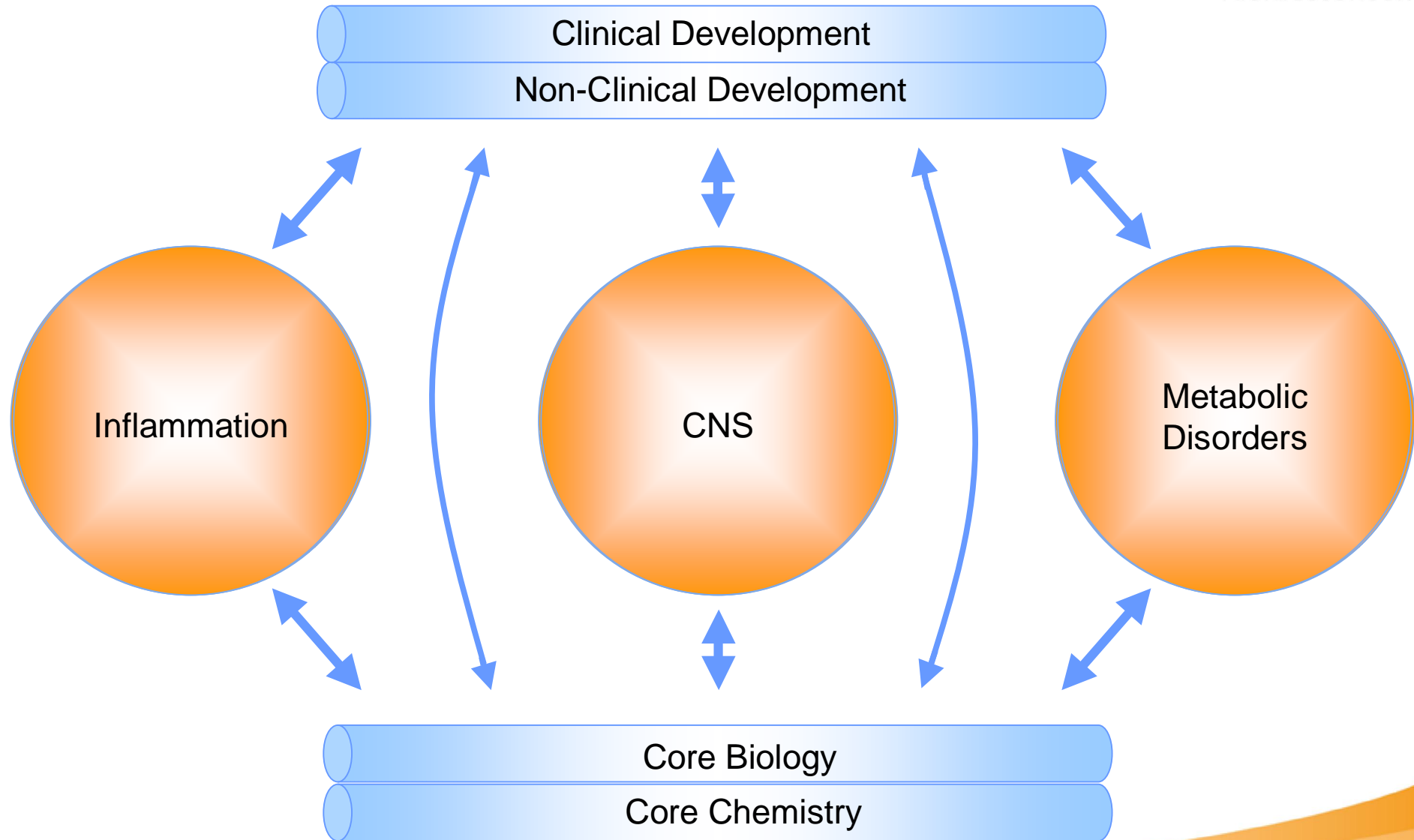


Allostery preserves natural rhythm



- Allosteric modulators often have greater specificity than orthosteric molecules
- Non-competitive mechanism means lower doses (more convenient/cheaper)
- Alter receptor activity without turning it on/off (less tolerance/desensitization)
- Can target receptors currently only addressed by peptides/proteins (COGs/oral)

The Addex Platform



www.addexpharma.com

allosteric modulators for human health

