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-LID starts 2H09
  - 12 preclinical programs
- Validating deals with Merck & Co. and Johnson & Johnson

Financials

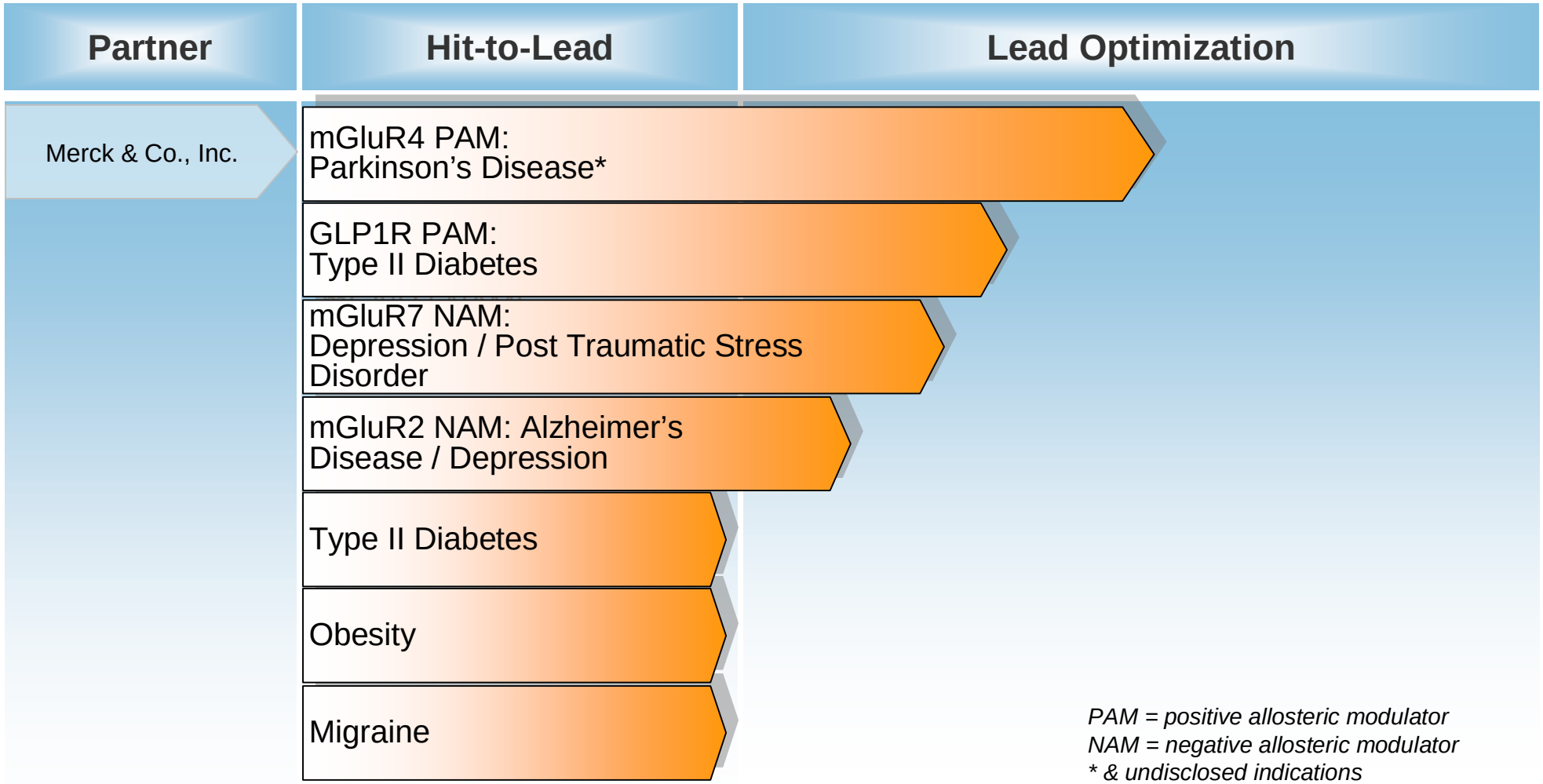
- Cash at 31 Dec 2008: CHF119.5 m
- 2009 cash burn guidance: CHF40-45m
- Market cap (28 Feb 09): CHF188m (€126 / US$161)
- SIX Swiss Exchange: ADXN (ISIN:CH0029850754)
- Five analysts set price targets from CHF34-70

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



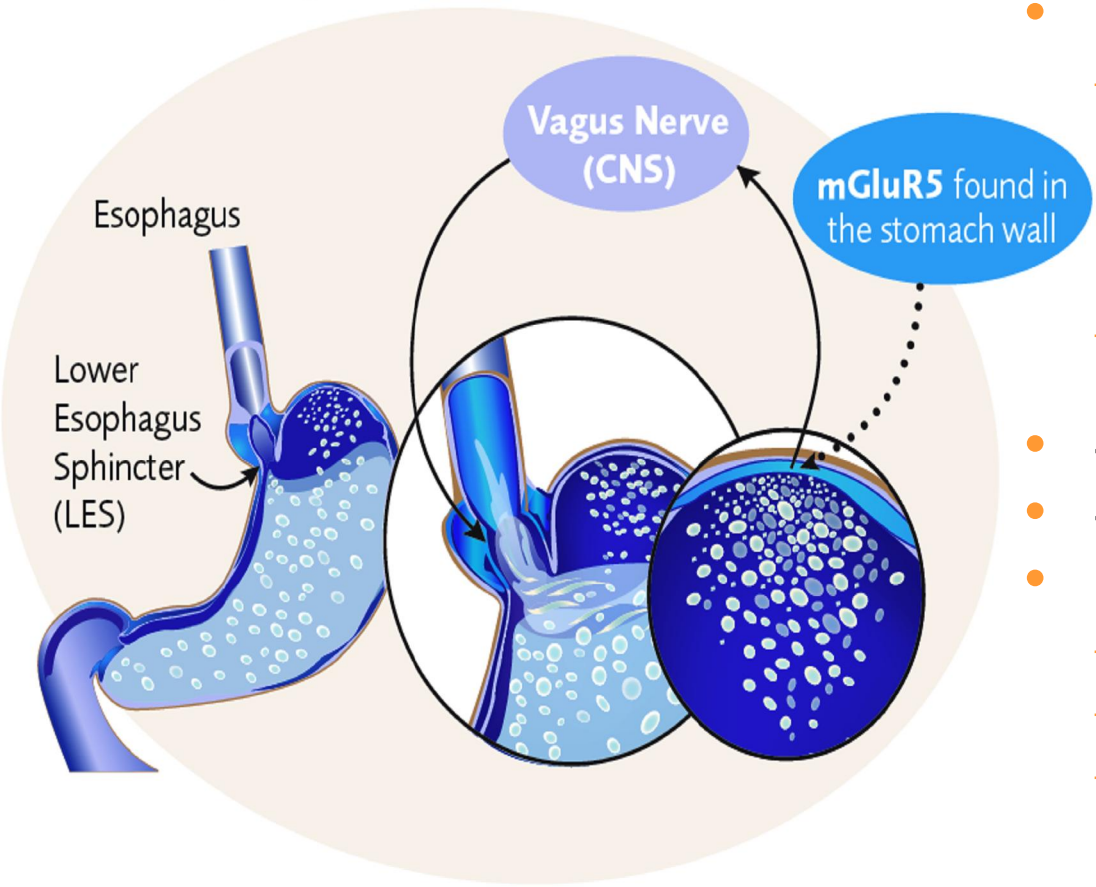
PAM = positive allosteric modulator
NAM = negative allosteric modulator
** & undisclosed indications*

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

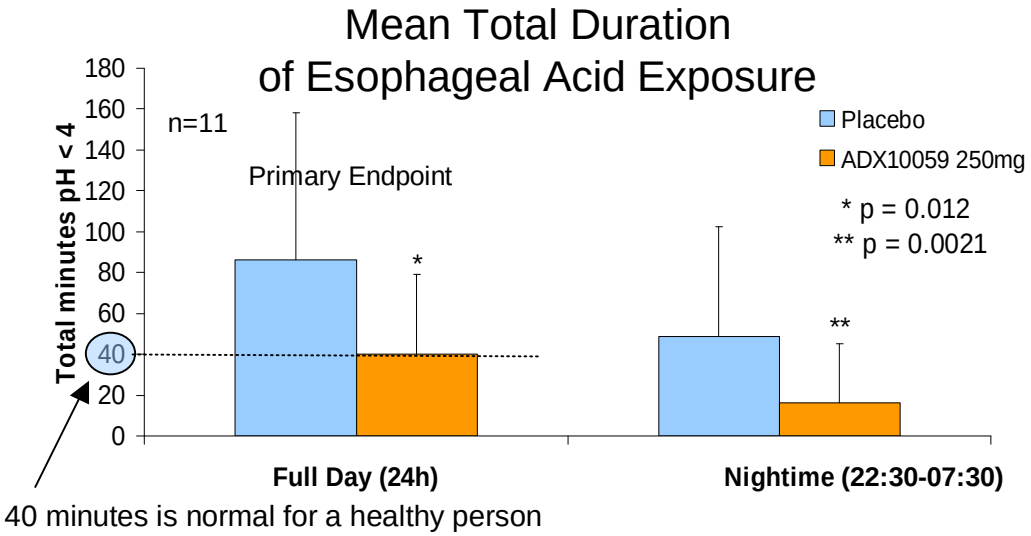
* research funding received from J&J: €4.2 million
** & other undisclosed indications

ADX10059 in GERD (Gastroesophageal Reflux Disease)

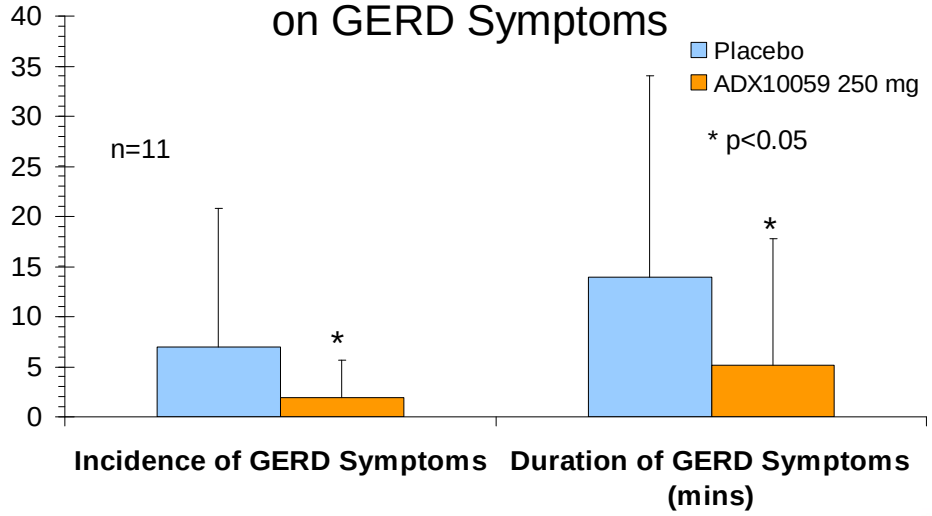


- **GERD is not caused by too much acidity**
- **GERD is due to poor lower esophageal sphincter (LES) function**
- **mGluR5 in GERD**
  - **metabotropic glutamate receptor 5 (mGluR5)**
    - Ø **found in stomach wall**
    - Ø **Act as "stretch sensors"**
    - Ø **regulate, via vagus nerve, LES function**
  - **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



40 minutes is normal for a healthy person



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 esophagous
  - drop in pH is a surrogate measure of reflux

- Secondary endpoints:
  - nightime 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)

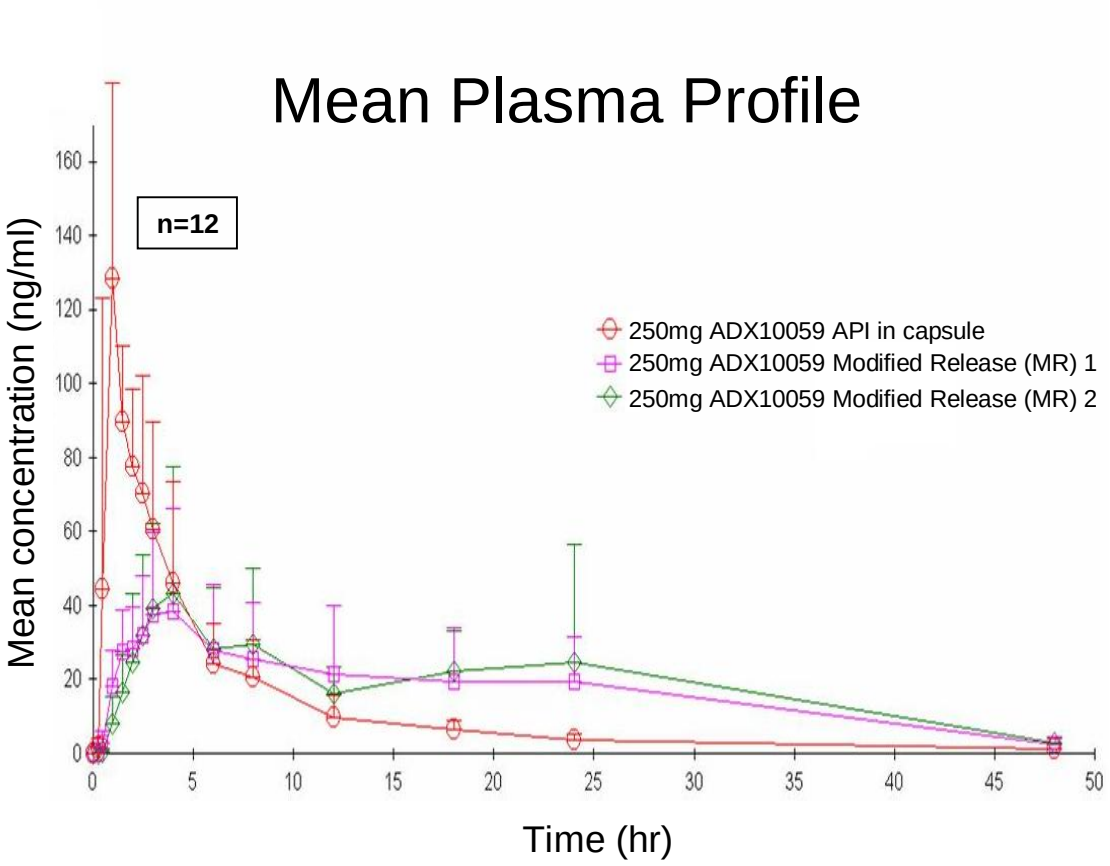
Design: single-dose, three-way crossover comparing

- 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



- 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)

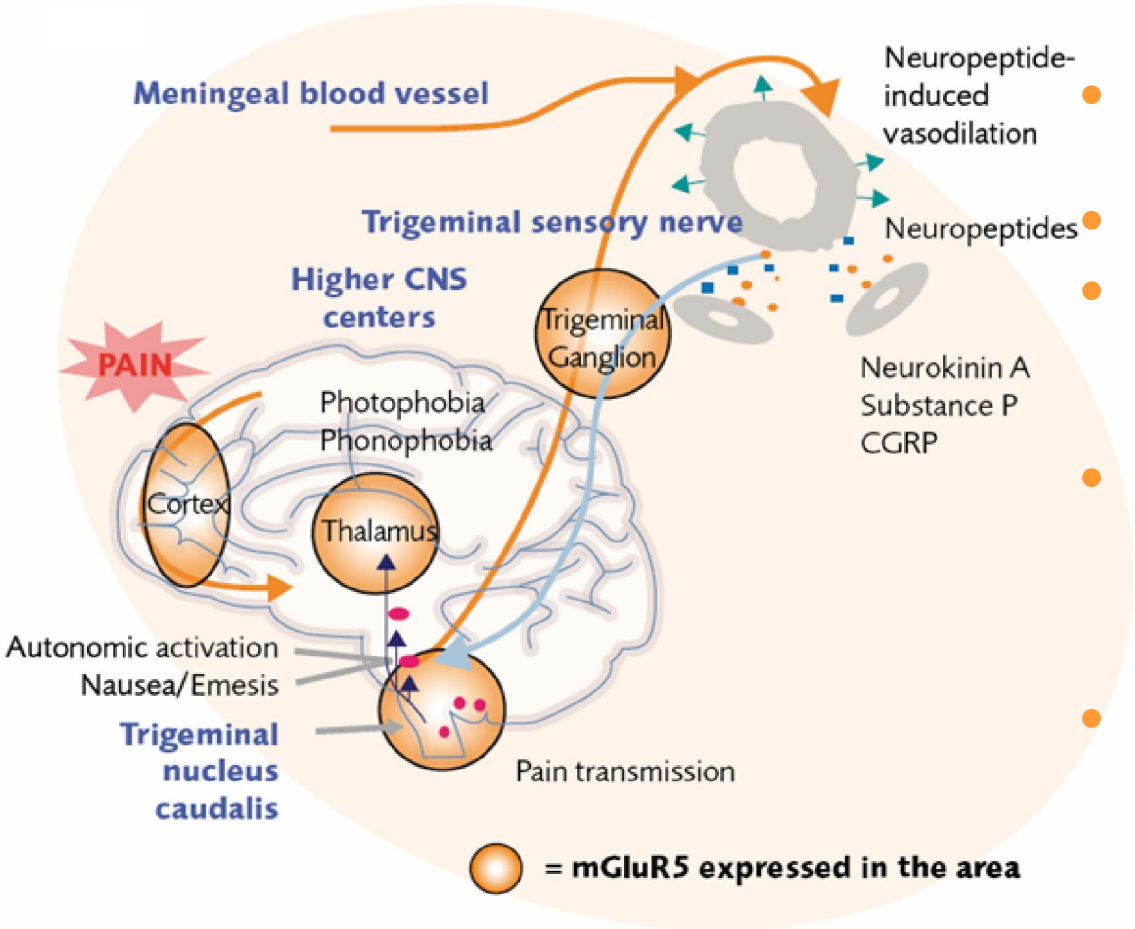
Started Dec' 08

- 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

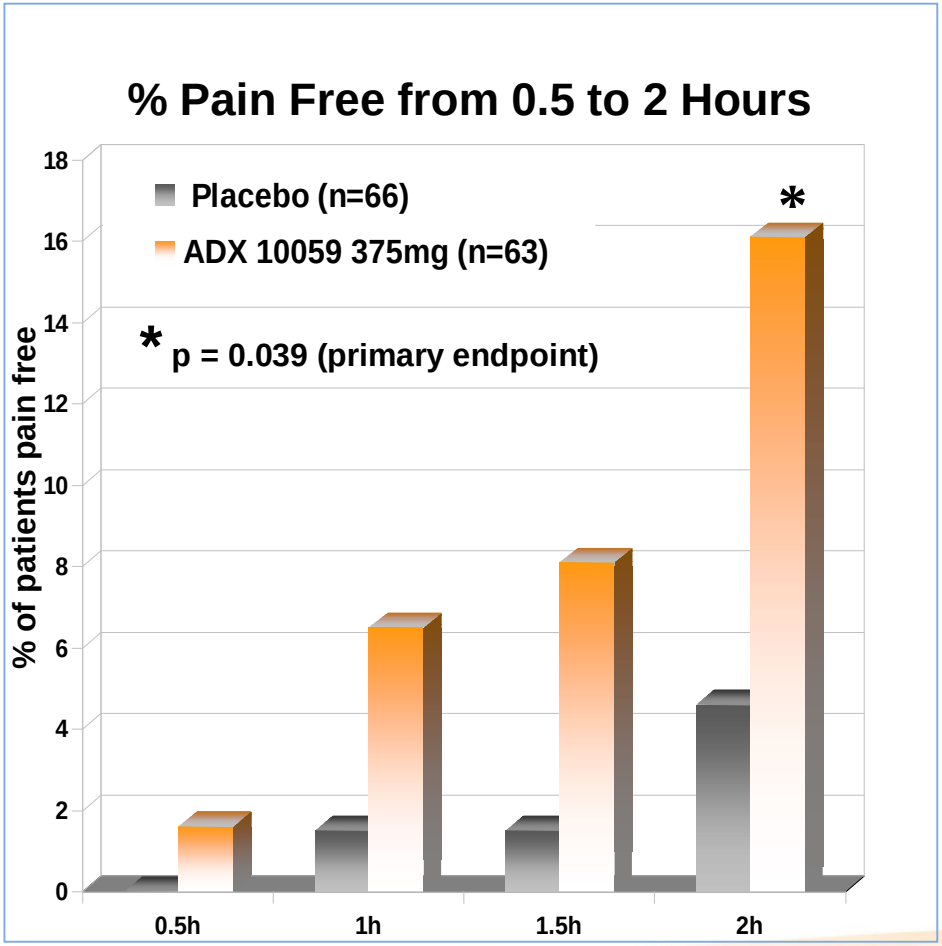


- The “migraine circuit” is a positive feedback loop leading to inflammation, pain, etc.
- Glutamate mediates relays in migraine circuit
- mGluR5 is in migraine circuit brain regions
- 12% prevalence (~30 million U.S. patients)
  - ~25% of migraneurs have 3+ attacks/month
  - avoiding migraines is better 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

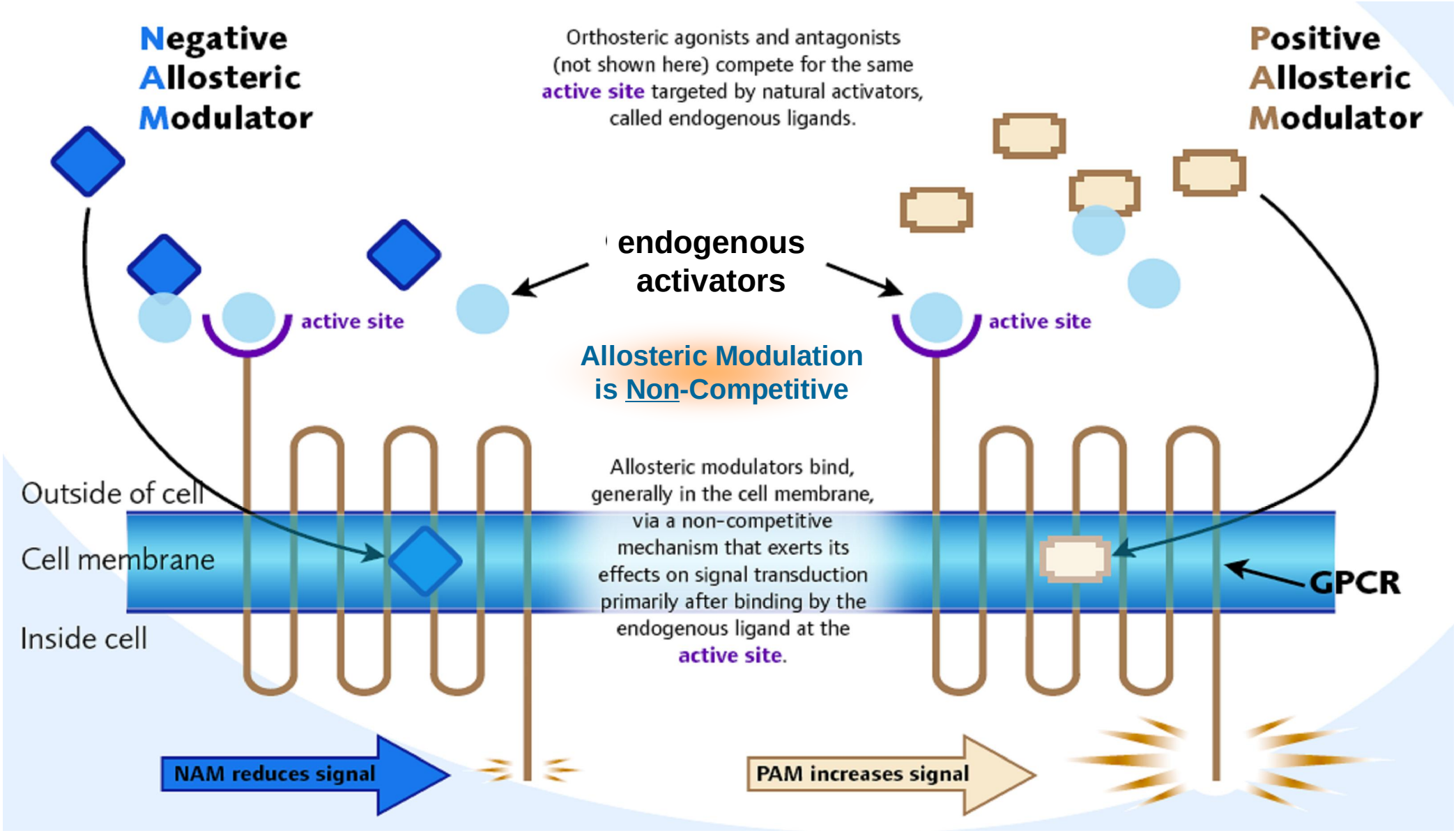
Product	Trial	Objectives	When
ADX10059	Phase IIb	GERD symptom control as monotherapy (study ADX10059-204)	data 2H09
ADX10059	Phase IIb	GERD symptom control as an add-on to PPIs (study ADX10059-205)	data 2H09
ADX10059	Phase IIb	reduce migraine frequency and severity (study ADX10059-206)	data 1H10
ADX48621	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

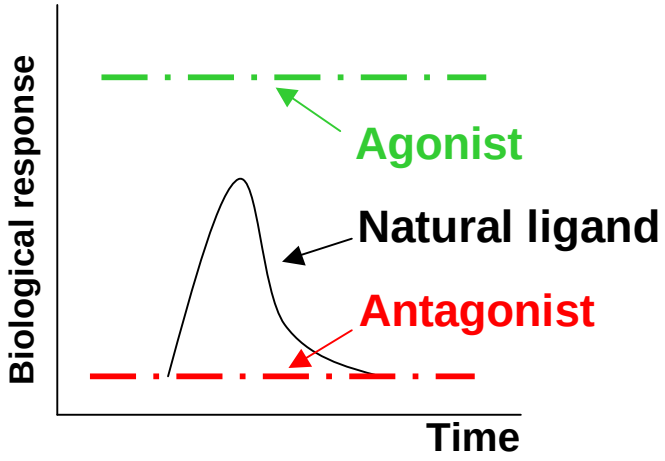
- Glutamate is *the* major neurotransmitter
- Even after 30 years, most attempts to drug glutamate receptors fail
- Knowledge about the functioning of $mGluR_{1\text{-}8}$ has been accumulated
- To drug mGluRs Addex pioneered tools for allosteric modulator discovery
  - Addex has built a proprietary 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

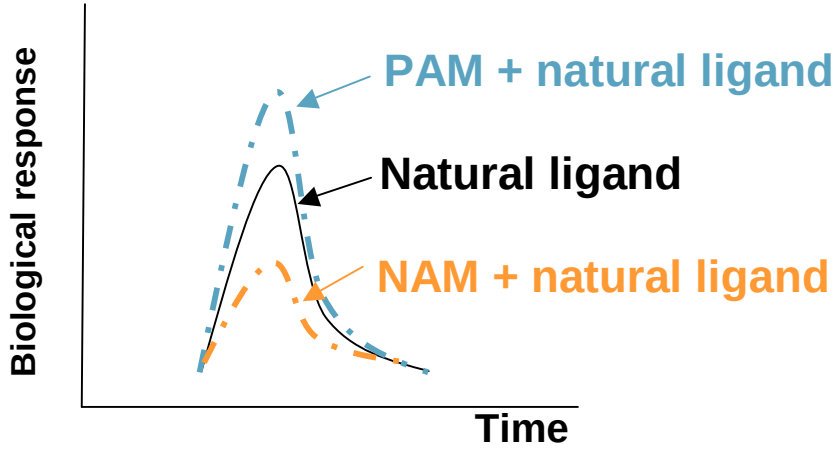


Orthosteric ≠ Allosteric

Orthosterics are steady state

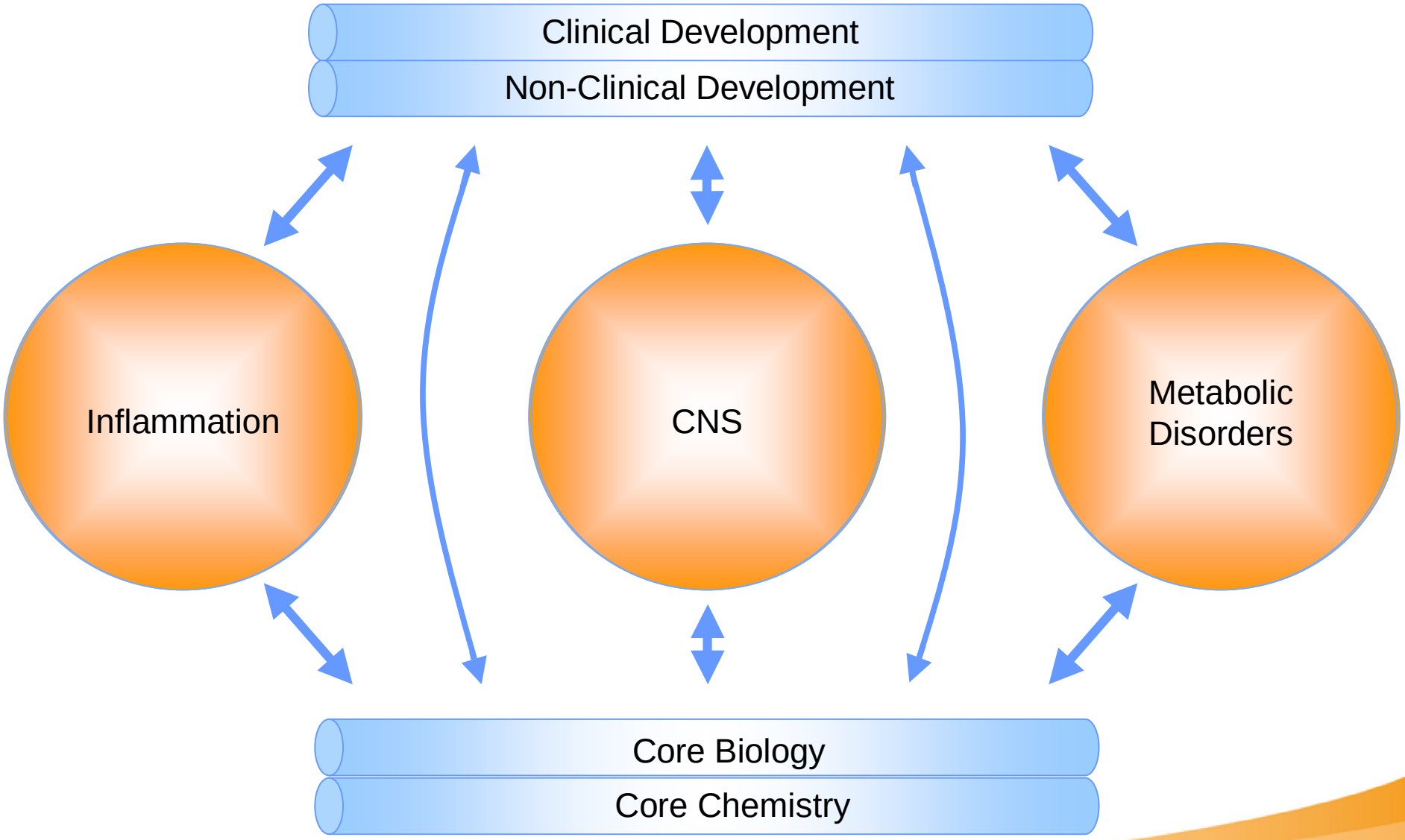


Allostery preserves natural rhythm



- 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



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