



Addex and Merck & Co., Inc.

the mGluR5 PAM deal



Agreement



- Merck received an exclusive license to develop Addex' ADX63365 and associated backup compounds
- ADX63365 is a metabotropic glutamate receptor 5 (mGluR5) positive allosteric modulator (PAM)
- ADX63365 is a drug candidate for schizophrenia and other conditions
- Merck is responsible for clinical development
- Addex will participate on a joint oversight committee
- Schizophrenia is the first indication, additional indications are undisclosed
- Addex has received an option to co-promote in certain EU countries



Financial Terms



- Addex receives \$22 million upfront
- Addex is eligible to receive \$455 million in research, development, regulatory and sales milestones for the first product in two indications
- Addex is eligible for an additional \$225 million in development, regulatory and sales milestones for a second product in two indications
- Addex is eligible for undisclosed royalties



Financial Guidance



- Full year unaudited cash burn for 2007 is CHF37.7m
 - Operating cash burn is CHF35.0m
 - Capex cash burn is CHF2.7m
- Full year cash burn guidance for 2008 is CHF25 to 30 million
 - Operating cash burn of CHF20 to 23m
 - Capex cash burn of CHF5 to 7m

Schizophrenia

Schizophrenia



Schizophrenia is a chronic, severe, and disabling brain disease

Epidemiology

- Affects ~ about 1.1% of the U.S. population over 18, according to NIMH
- Appears in the late teens to early thirties (earlier in males)
- Estimates suggest that no more than one in five individuals recovers completely

Symptoms

- Positive symptoms include: delusions, hallucination, neurosis
- Negative symptoms include: depression and anti-social behavior
- Cognitive dysfunction: excludes young patients from higher education or jobs

Marketed drugs (D2 blockers) offer value but do not reverse cognitive dysfunction

- Eli Lilly 2007 olanzapine sales are expected to be ~\$4.5 billion
- J&J 2007 risperidone sales are expected to be ~\$4.5 billion
- Side effects with D2 blockers: weight gain, extrapyramidal symptoms & hyperprolactinemia



mGluR5 PAM in Schizophrenia

mGluR5 in Schizophrenia



- In preclinical testing, mGluR5 activation has shown anti-psychotic effects similar to marketed drugs
- Anti-psychotic effect allows pursuit of first-line monotherapy label
 - Novel mechanism suggests the possibility of avoiding side effects associated with poor compliance with currently marketed drugs:
 - weight gain
 - extrapyramidal symptoms (EPS)
 - hyperprolactinemia
 - Combination with marketed products possible
- mGluR5 activation reverses cognitive dysfunction in preclinical models
 - Preclinical data have been published by Merck & others
 - Marketed products do not reverse cognitive decline
- Additional efficacy on negative symptoms to be evaluated



mGluR5 PAM & mGluR2 PAM

different approaches to treating Schizophrenia

mGluR2 & mGluR5 PAM



- mGluR2/3 activation is clinically validated in schizophrenia (and anxiety)
 - mGluR2/3 agonist efficacious on positive and negative symptoms of schizophrenia
 - mGluR2/3 agonist efficacy similar to olanzapine BUT:
 - no weight gain
 - no EPS
 - no hyperprolactinemia
- mGluR5 rationale is very strong
 - mGluR5 is linked to NMDA receptor function
 - NMDA shown in humans to induce schizophrenia symptoms
 - mGluR5 PAM has demonstrated effects in animal models of schizophrenia
 - for positive symptoms
 - for cognition

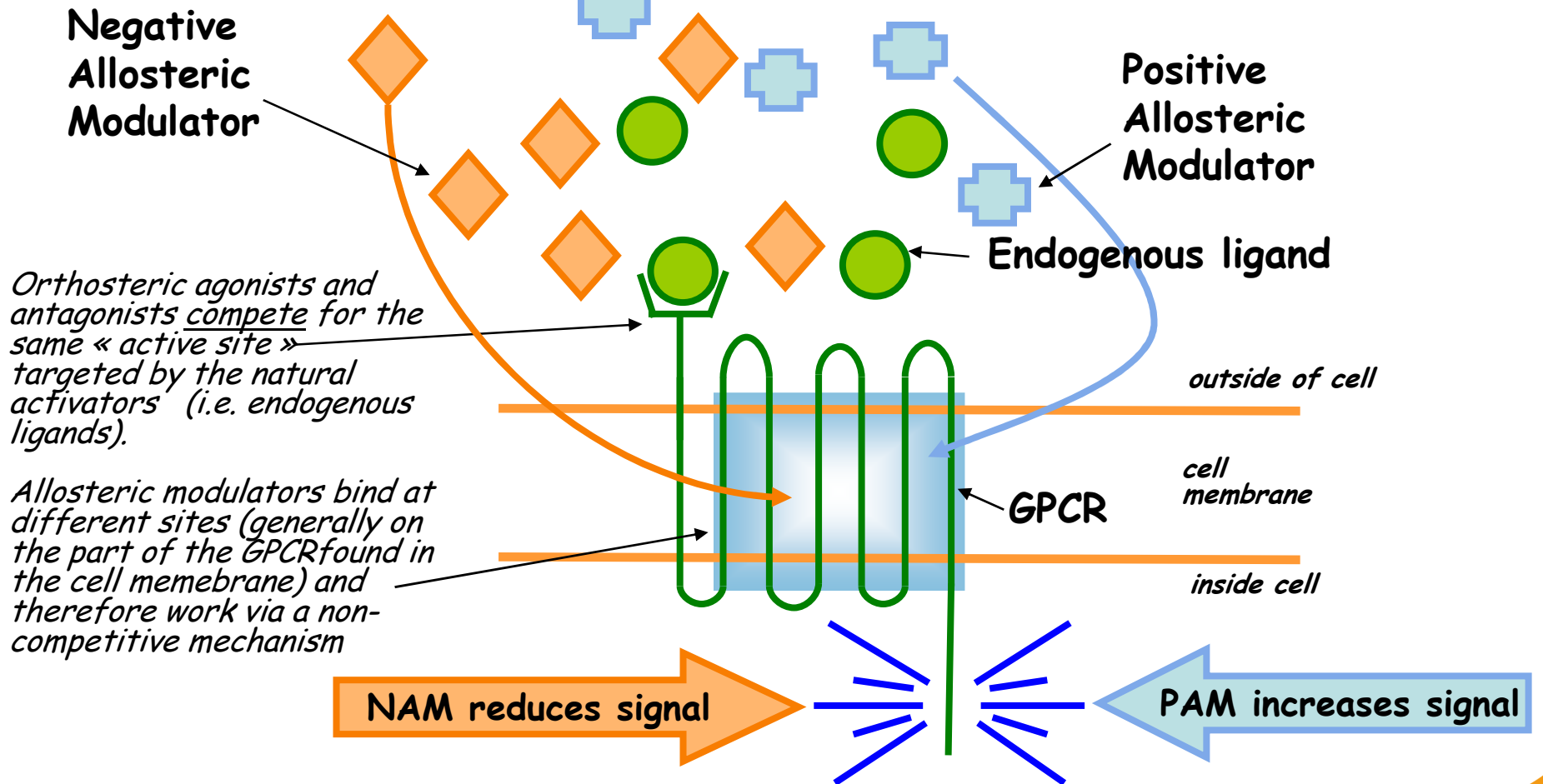


Allosteric Modulators

Addex' goal is to become a world class pharmaceutical company

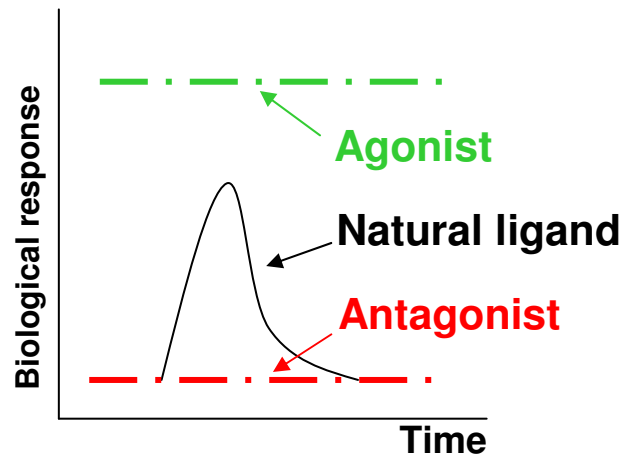
Allosteric Modulation

~a non-competitive approach~

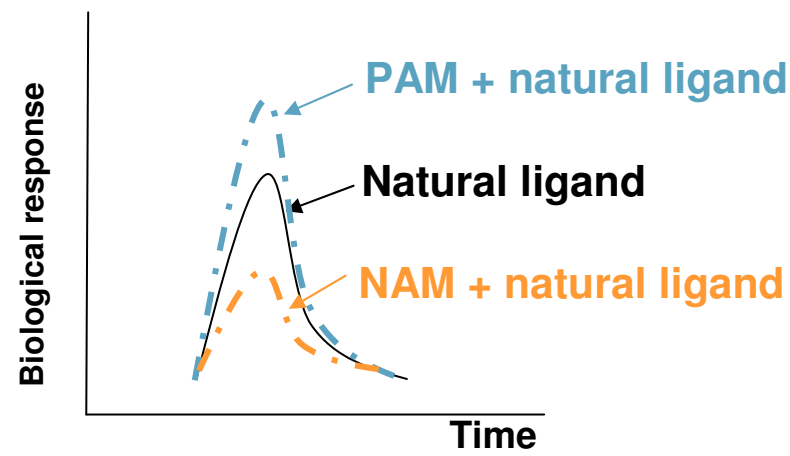


Orthosteric \neq Allosteric

Orthosterics are steady state



Allostery preserves natural rhythm



- PAMs & NAMs do not activate/deactivate receptors – the natural ligand does
- Natural physiological rhythm may mean fewer side effects and/or better efficacy
- Addex chemists can fine tune how much a PAM/NAM turns the signal up/down
- “Dimmer switch” approach offers more sophisticated therapeutic strategies

Addex can target all GPCR Families



Family 1		Family 2	
<p>1a</p>	<p>Muscarinic receptors Odorants Catecholamines Adenosine Opioid receptors Anandamide</p>		<p>Calcitonin PTH VIP PACAP GnRH CRF GLP-1 Glucagon GIP</p>
<p>1b</p>	<p>Peptides Cytokines II₈ Formyl Met-Leu-Phe fMLP-peptide PAF-acether Thrombin</p>		
<p>1c</p>	<p>Glycoproteins hormones (LH, TSH, FSH)</p>		
		Family 3	
			<p>mGluR1-8 Ca⁺⁺ GABA_B Pheromones (VR, G_oVN)</p>

Adapted from Bockaert & Pin, EMBO J, 1999



Addex Pipeline

Allosteric Modulator Pipeline



Discovery	Preclinical	Phase I	Phase IIa	Milestones	Partner
ADX10059 (metabotropic glutamate receptor 5 NAM) Gastroesophageal Reflux Disease (GERD)				Ph IIa endpoint met Ph IIb start: mid 2008	<i>To be partnered after Ph IIb</i>
ADX10059 (mGluR5 NAM) Migraine Prevention				Ph IIa endpoint met Ph IIb start: mid 2008	
ADX48621 (mGluR5 NAM) Depression & Anxiety				Ph I data: 2008	<i>To be partnered</i>
ADX63365 (mGluR5 PAM) Schizophrenia					Merck & Co.
ADX71441 (GABA _B PAM) Spasticity/GERD/Anxiety				Ph I start: 4Q08 / 1Q09	
ADX68693 (FSH NAM) Contraception / Osteoporosis				Phase I start: 2009	<i>To be partnered</i>
mGluR2 PAM Schizophrenia/Anxiety					Johnson & Johnson
mGluR4 PAM Parkinson disease					Merck & Co.
GLP1R PAM Type II Diabetes					<i>To be partnered after Ph IIb</i>
GPCR1 NAM Depression					<i>To be partnered</i>
GPCR2 NAM Depression					<i>To be partnered</i>

NAM = negative allosteric modulator
PAM = positive allosteric modulator



Deals Bring More Validation for Addex

The Four Major Validations for Addex' Allosteric Modulator Platform



- 1) Finding drug-like mGluR5 PAMs has been challenging for pharma. This deal provides Merck exclusive rights to Addex' ADX63365, a selective mGluR5 PAM, as well as multiple backup compounds
- 2) Finding drug-like mGluR4 PAMs has been challenging for pharma. Merck and Addex signed a separate deal in early December to discover and develop selective mGluR4 PAMs for Parkinson's disease
- 3) Finding drug-like mGluR2 PAMs has been challenging for pharma. Addex signed in 2004 a deal with Johnson & Johnson to discover and develop selective mGluR2 PAMs for schizophrenia and anxiety
- 4) ADX10059, an mGluR5 negative allosteric modulator (NAM), has met primary endpoints, achieving clinical proof of concept, in both migraine and gastroesophageal reflux disease (GERD)



allosteric modulators for human health

Q&A

www.addexpharma.com