

## EXECUTIVE SUMMARY



**Addex Pharmaceuticals** ([www.addexpharma.com](http://www.addexpharma.com)) discovers and develops allosteric modulators for human health and is focused on validated therapeutic targets in diseases of the central nervous system, metabolic disorders and inflammation. Phase II clinical trials are scheduled to start around the end of 2010 for two lead products in four indications: ADX48621, an mGluR5 negative allosteric modulator (NAM), in dystonia and Parkinson's disease levodopa-induced dyskinesia (PD-LID); and ADX71149, an mGluR2 positive allosteric modulator (PAM), in schizophrenia and anxiety. ADX71149 is licensed to Ortho-McNeil-Janssen Pharmaceuticals Inc., a Johnson & Johnson company. A third product, ADX71943, GABA-B receptor PAM with potential for chronic pain, is scheduled to enter Phase I testing in 2011. In addition, Merck & Co., Inc. has licensed rights to two preclinical products: mGluR4 PAM for Parkinson's disease and mGluR5 PAM for schizophrenia. Additional preclinical discovery stage programs include: GLP1R PAM, GIPR PAM, IL1R1 NAM and TNFR1 NAM. Roche Venture Fund and SR-One, the corporate venture arm of GlaxoSmithKline, are investors in Addex.

**Shares** in Addex trade on the SIX Swiss Exchange main board under the stock symbol ADXN (ISIN: CH0029850754). There were 5,871,242 ADXN shares outstanding as of June 30, 2010. Addex had CHF56.7 million in cash as of June 30, 2010 and can fund operations through early of 2012. Founded in 2002 in Geneva, Switzerland, Addex has a subsidiary in Archamps, France, and employs about 120 people.

## PIPELINE

Molecule / Mechanism	Partner	Assay Dev Screening	Hit-to-Lead	Lead Opt	Preclinical	Phase I	Phase II	Milestone
<b>ADX48621</b> mGluR5 NAM		Parkinson's Disease Levodopa Induced Dyskinesia (PD-LID)						Start Ph II 4Q10
		Dystonia						Start Ph IIa 1Q11
<b>ADX71149</b> mGluR2 PAM	Ortho-McNeil-Janssen	Schizophrenia				funded & developed by OMUPI*		Start Ph IIa 1Q11
	Ortho-McNeil-Janssen	Anxiety				funded & developed by OMUPI*		Start Ph IIa 1Q11
<b>ADX71943</b> GABA-B PAM		Osteoarthritic Pain						Start Ph I 2011
<b>ADX63365</b> mGluR5 PAM	Merck & Co., Inc.	Schizophrenia ‡				funded & developed by Merck		
<b>ADX68692</b> FSHR NAM		Endometriosis / Benign Prostatic Hyperplasia						

## DISCOVERY PROGRAMS

mGluR2 NAM		Alzheimer's / Depression						
mGluR4 PAM	Merck & Co., Inc.	Parkinson's Disease ‡				funded by Merck		CNS
mGluR7 NAM		Depression Post Traumatic Stress Disorder						
Orexin 2R NAM		Sleep Disorders						
GLP1 PAM		Type II Diabetes					Metabolic Disorders	
GIPR PAM		Type II Diabetes						
TNFR1 NAM (CD120a)		Rheumatoid Arthritis, Psoriasis, Alzheimer's, Multiple Sclerosis					Inflammation	
A2A PAM		Psoriasis, Osteoarthritis						
IL1R1 NAM (CD121a)		Gout, Type II Diabetes						

○ **NAM** = negative allosteric modulator (an inhibitor)    ‡ and undisclosed additional indications  
○ **PAM** = positive allosteric modulator (an activator)    \* Ortho-McNeil-Janssen Pharmaceuticals, Inc., a Johnson & Johnson subsidiary

### Management

### Board of Directors

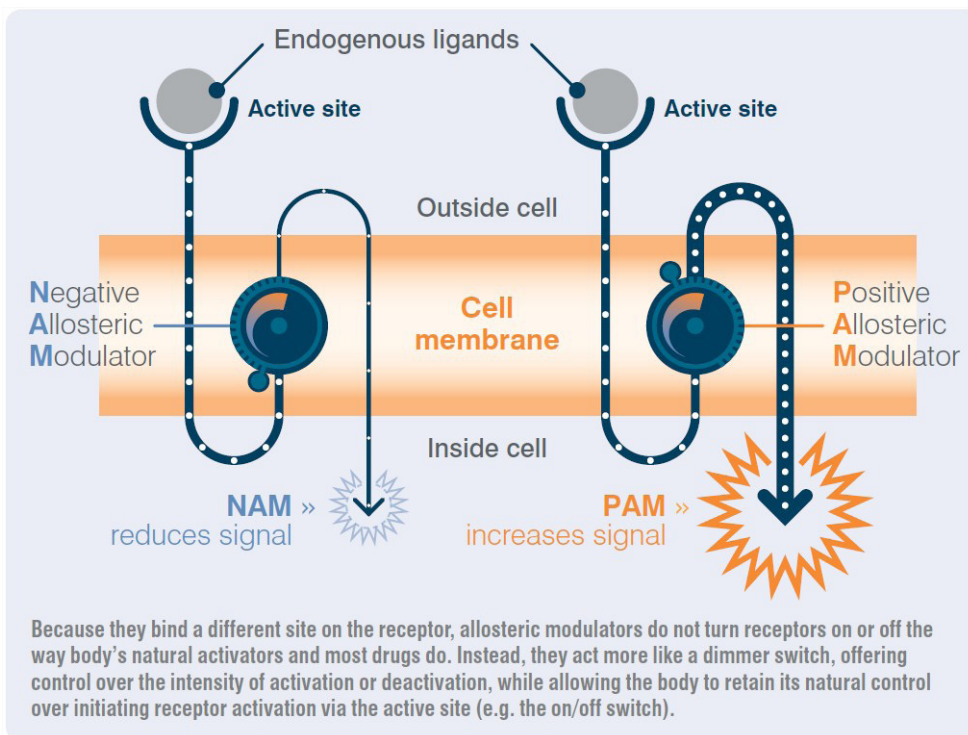
- Vincent Mutel, *Chief Executive Officer*
- Tim Dyer, *Chief Financial Officer*
- Charlotte Keyword, *Chief Medical Officer*
- Sonia Poli, *Head of Non-Clinical Development*
- Laurent Galibert, *Head of Inflammation / Metabolic Disorders*
- Jean-Philippe Rocher, *Head of Core Chemistry*
- Robert Lütjens, *Head of Core Biology*
- Tatiana Carteret, *Head of Human Resources*
- Chris Maggos, *Head of Investor Relations & Communications*

- André J. Mueller, *Chairman*
- Vincent Mutel, *Vice Chairman & CEO*
- Andrew Galazka, *SVP Scientific Affairs, Merck-Serono*
- Ray Hill, *former Head of EU Licensing, Merck & Co., Inc.*
- Vincent Lawton, *former MD of Merck Sharp & Dohme U.K.*
- Beat E. Lüthi, *CEO of CTC Analytics*
- Antoine Papiernik, *Sofinnova Partners*

## Allosteric modulation explained

**Allosteric modulators** are an emerging class of orally available small molecule therapeutic agents that may offer a competitive advantage over classical drugs. This potential stems from their ability to offer greater selectivity and better modulatory control at disease mediating receptors. Most marketed drugs bind receptors where the body's own natural molecular activators (i.e. endogenous ligands) bind, specifically to a key part of each receptor's anatomy called the "active site". In short, most drugs must out-compete endogenous ligands for the active site.

By contrast, allosteric modulators are non-competitive because they bind receptors and modify receptor function even if the endogenous ligand also is binding it. Because of this, allosteric modulators aren't limited to simply turning a receptor on or off, the way most drugs are. Instead, they act more like a dimmer switch, offering control over the degree of activation or deactivation, while allowing the body to retain its natural control over initiating receptor activation. Furthermore, with regard to the structural diversity of invented compounds, the allosteric approach generally affords freedom to operate – even on well-known, clinically validated targets – because the intellectual property surrounding allosteric compounds and the allosteric sites on receptors is most often un-exploited



### Key properties & advantages of allosteric modulation:

- Allosteric modulators bind their target at a different site from endogenous ligands and therefore are most influential only when the endogenous ligand is bound to its site on the same target at the same time. By contrast, classical orthosteric drugs compete for the same site as endogenous ligands. As results, lower affinity allosteric modulators may be effective where a similar affinity orthosteric modulator is not. Thus, allosteric modulators may have fewer side effects due to off-target activities compared to classical orthosteric drugs against the same target.
- Allosteric modulators often are devoid of activity in the absence of endogenous ligands. Because of this, they preserve the natural biological rhythms compared to orthosteric approaches. This could lead to greater safety and fewer side effects compared to classical orthosteric drugs against the same target.
- Because allosteric modulators bind on a different site compared to classical orthosteric drugs, Addex can create new chemical entities that re-address clinically validated targets – potentially offering improved therapeutic activity without being blocked by existing intellectual property.
- For targets where it has been difficult to make selective orthosteric drugs highly selective allosteric modulators can sometimes be identified. For example, Addex has made orally available small molecule allosteric modulators against the GLP-1 receptor, the FSH receptor or TNF receptor – for which only peptide or hormonal therapies are available.
- It is possible to combine allosteric modulators with orthosteric drugs. For example a PAM could be used to potentiate an orthosteric agonist.

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