

Addex Pharmaceuticals (SIX:ADXN) discovers and develops allosteric modulators for human health. Allosteric modulators are a different kind of orally available small molecule therapeutic agent, which we believe will offer a competitive advantage over classical drugs. The lead product in our pipeline, ADX10059, has achieved clinical proof of concept and is in Phase IIb testing for the treatment of GERD (e.g. heartburn) and, separately, migraine headache. Both are important diseases for which existing products have established multi-billion dollar markets despite sub-optimal efficacy. ADX10059 is a first-in-class mGluR5 inhibitor, a cutting edge therapeutic strategy that also is being pursued by large pharma competitors in multiple indications with unmet medical need.

Our technology and products already have proven their value through our relationships with four of the top ten pharmaceutical companies in the world. Specifically, in two separate agreements with *Merck & Co., Inc.*, signed in December 2007 and January 2008, we are developing allosteric modulators as drugs to treat Parkinson's disease and schizophrenia, respectively. A third agreement, with *Johnson & Johnson*, is focused on development of allosteric modulators to treat anxiety and schizophrenia. Separately, the investment funds of *Roche* and *GlaxoSmithKline* have extended their validation of our technology, products and management by making significant investments in Addex.

Founded in 2002 in Geneva, Switzerland, Addex has a subsidiary in Archamps, France, and employs about 145 people.

Shares in Addex trade on the SIX Swiss Exchange main board under the stock symbol ADXN (ISIN: CH0029850754). There were 5,862,492 ADXN shares outstanding as of December 30, 2008. Addex had CHF119.5 million in cash as of December 30, 2008 and can fund operations through at least early 2012.

Although, initially, focused only on CNS indications, Addex has chosen to focus on three core disease areas: CNS, metabolic disorders and inflammation. The most advanced drug candidate, **ADX10059**, a metabotropic glutamate receptor 5 (mGluR5) negative allosteric modulator (NAM), is in Phase IIb testing and has met the primary endpoints in separate Phase IIa trials in migraine and gastroesophageal reflux disease (GERD) patients, demonstrating clinically and statistically significant efficacy for both diseases. **ADX48621**, an mGluR5 NAM, has successfully completed the Phase I and will be developed to treat Parkinson's disease levodopa induced dyskinesia (PD-LID). It also can serve as a backup for ADX10059 in GERD and migraine.

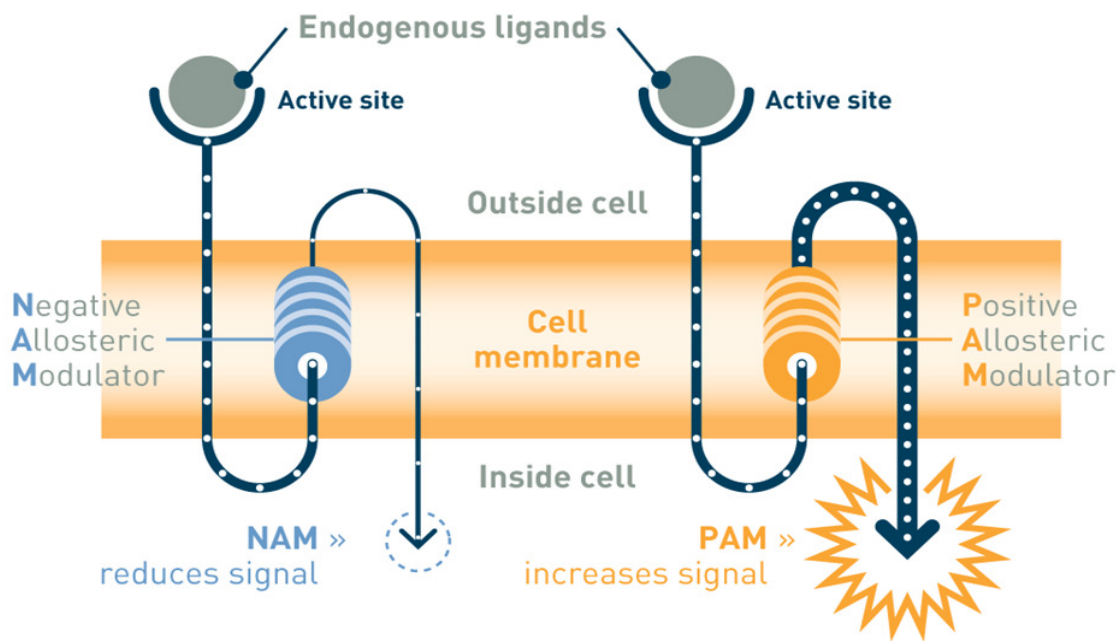
Screening & Hit-to-Lead	Lead Optimization	Preclinical	Phase I	Phase IIa	Phase IIb	Milestone / Partner
ADX10059 (mGluR5 NAM) monotherapy in PPI responders (study 204): Gastroesophageal Reflux Disease (GERD)						Data 2H09
ADX10059 (mGluR5 NAM) add-on in PPI partial responders (study 205): GERD						Data 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)						Ph IIa start 2H09
ADX71149 (mGluR2 PAM): Anxiety / Schizophrenia						Ortho-McNeil-Janssen Pharmaceuticals (J&J)
ADX63365 (mGluR5 PAM): Schizophrenia*						Merck & Co., Inc.
ADX71943 (GABAB PAM): Pain / UI / GERD						Ph I start 1H10
ADX68692 (FSH NAM): Contraception / Osteoporosis						
Adenosine A3 Antagonist : Glaucoma						
mGluR4 PAM: Parkinson's Disease*						Merck & Co., Inc.
GLP-1R PAM: Type II Diabetes						
mGluR7 NAM: Depression / Post Traumatic Stress Disorder						
mGluR2 NAM: Alzheimer's Disease / Depression						
Type II Diabetes						
Obesity						
Migraine						

Preclinical: **ADX63365**, an mGluR5 positive allosteric modulator (PAM) for schizophrenia & cognitive impairment; **ADX71943**, a GABA_B receptor PAM, with potential for GERD, urinary incontinence & pain; **ADX71149**, an mGluR2 PAM (partnered with J&J's Ortho-McNeil-Janssen), for anxiety & schizophrenia; **ADX68692**, a NAM of follicle stimulating hormone (FSH) receptor, for contraception. Other early programs address targets for Parkinson's disease, depression, diabetes and other diseases.

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

Allosteric modulators are an emerging class of orally available small molecule therapeutic agents that we believe will offer patients better results than 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, the allosteric approach generally affords freedom to operate – even on well-known, clinically validated targets – because the intellectual property surrounding allosteric chemistry and the allosteric sites on receptors is most often un-exploited.

Orthosteric agonists and antagonists (not shown here) compete for the same “active site” targeted by natural activators, called endogenous ligands.



Allosteric modulators bind , generally in the cell membrane, ia a non-competitive mechanism that exerts its effects on signal transduction primarily after binding by the endogenous ligand at the active site.

Key properties & advantages of allosteric modulation:

- Allosteric modulators bind their target at a different site from endogenous ligands and therefore are most influential when an endogenous ligand is bound to another 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 dose/affinity allosteric modulators may be effective where a similar dose/affinity orthosteric modulator is not. Thus, allosteric modulators may have fewer side effects due to off target activities than 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 biology 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 GPCR 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 and the FSH 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.

Management

- **Vincent Mutel**, Chief Executive Officer
- **Tim Dyer**, Chief Financial Officer
- **Charlotte Keywood**, Chief Medical Officer
- **Sonia Poli**, Head of Non-Clinical Development
- **Emmanuel Le Poul**, Head of CNS Business Unit
- **Laurent Galibert**, Head of Inflammation Business Unit
- **Laurent Massuyeau**, Head of Business Development
- **Jean-Philippe Rocher**, Head of Core Chemistry
- **Robert Lütjens**, Head of Core Biology
- **Chris Maggos**, Head of Investor Relations & Communications

Board of Directors

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- **Vincent Mutel**, Vice Chairman & CEO
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- **Andrew Galazka**, SVP Scientific Affairs, Merck-Serono
- **Antoine Papiernik**, Sofinnova Partners
- **Vincent Lawton**, former VP of Merck Sharp & Dohme
- **Beat E. Lüthi**, CEO of CTC Analytics

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