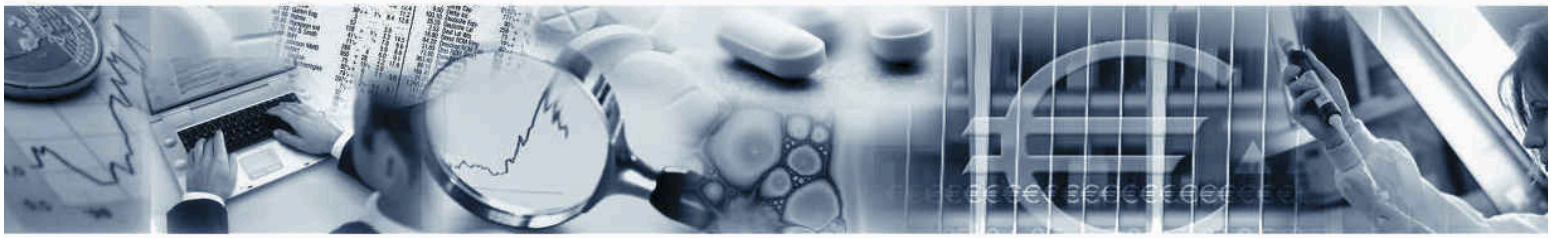

Research Note

Addex Therapeutics

Luctor et Emergo

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Date: 8 June 2016

Name:	**Addex Therapeutics**
Country:	**Switzerland**
Price:	**CHF 2.32**
ISIN Code:	**CH0029850754**
Reuters Code:	**ADXN.SW**
Market Cap (CHF m):	**27.6**
EV (CHF m):	**25.0**
Cash & cash eq. (CHF m):	**2.6**
Shares outstanding (m):	**11.7**
Volume:	**17,740**
Free float:	**89.6%**
52-week Range:	**2.15-3.69**

	2014A	2015A	2016E
Total Revenues	1.03	0.79	1.00
Net (Loss)/Profit	(1.77)	(4.20)	(6.00)
Net loss per share (cents)	(0.18)	(0.39)	(0.52)
R&D costs	0.9	1.78	7.50
Cash increase/(decrease)	(0.95)	0.70	10.00
Cash and marketable sec.	1.98	2.63	5.00

Executive Summary

- Addex Therapeutics is a Swiss based biopharmaceutical company that is developing innovative oral therapies with a focus on neurological disorders. Addex' lead program is in preparation to start a phase III study for levodopa-induced dyskinesia associated with Parkinson's disease (PD-LID). Addex has a proprietary small molecule allosteric modulator discovery platform. The company currently has 5 drug programs in or close to the start of clinical development and another 6 in preclinical development.

- The company's proprietary allosteric modulation technology offers significant advantages over classical drugs by demonstrating better pharmacological selectivity and safety profile at a similar level of efficacy. Also, allosteric modulators with lower potency can be effective in situations where a similar potency orthosteric modulator fails. Moreover, as Addex focuses specifically on those therapeutic targets that are clinically validated and whose existing products have well-established markets, the risk profile of its drug pipeline is relatively low.

- Addex' lead product is dipraglurant that successfully completed a phase IIa POC trial in Parkinson's disease levodopa induced dyskinesia (PD-LID). The drug is currently being prepared to enter a Phase III trial for PD-LID with the support from the Michael J Fox Foundation for Parkinson's Research. In addition to funding more than USD 600 million in research to date, the Foundation has fundamentally altered the trajectory of progress toward a cure.

- The Company's current cash position is CHF 2.6 million and we expect the company to raise additional funds in the near future or sign a lucrative partnering deal. This should be sufficient to carry out the further development of its pipeline and the important commencement of the Phase III trial with dipraglurant in PD-LID. Since its inception in

2002, the company raised CHF 280 million with the help of top tier investors from the US and Europe. In addition the company has received more than CHF50 million in cash inflows from partnering activities.

- Based on NPV based valuation, we believe that Addex Therapeutics is substantially undervalued at the current share price of CHF 2.32. Using our valuation model and taking into account the future revenues from its late stage clinical pipeline as well as potential partnerships, the company's current total value should be CHF 76 million, or CHF 6.50 per share. This represents a substantial upside from the current share price.

Company Profile & Technology

Addex Therapeutics is a Swiss based biopharmaceutical company that is developing an emerging class of oral small molecule drugs known as allosteric modulators. Allosteric modulators target a specific receptor or protein and alter the effect of the body's own signaling molecules on that target through a novel mechanism of action. The company enjoyed first-mover advantage in the process of discovering and developing allosteric modulators. Addex has developed an allostery-biased library of more than 70,000 compounds and biological assays which enable detection, optimization and confirmation of the mechanism of action of allosteric compounds.

Currently, Addex has a diverse pipeline of proprietary compounds that cater to a number of major diseases. The platform is broadly applicable and has generated several molecules for indications with significant commercial potential with a focus on central nervous system (CNS) disorders with orphan drug potential.

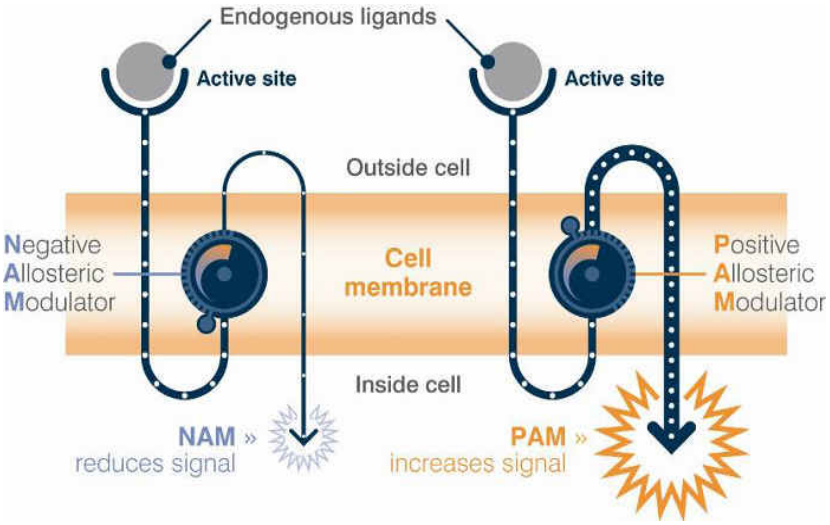
Allosteric modulation

Allosteric modulation is a mechanism to control the function of protein. This is done by binding an effector molecule, called allosteric modulator, at the protein's allosteric site i.e., at the site other than the protein's active site. Natural ligands, which are produced by the body, bind to a receptor's active site. Most of the available drugs compete with these natural ligands to bind to the active site. However, since allosteric modulators bind to the protein at a site other than the active site, they do not compete with the body's natural ligands. They can bind with the receptor even in the presence of natural ligand-receptor binding. As a result, allosteric modulators act as a dimmer switch controlling the level of activation or inhibition, rather than switching the receptor on or off, allowing the body to retain its natural control over receptor activation. The allosteric modulator affects the conformation of the receptor and hence changes its shape, and by doing so it affects the signals sent by the receptor intracellularly, resulting in the alteration of the

protein's activities.

There are two types of effectors:

- Allosteric activators: Effectors that increase the protein's activity.
- Allosteric inhibitors: Effectors that decrease the protein's activity.



Source: Addex Therapeutics

Advantages of allosteric modulation

Allosteric modulators with lower potency can be effective in situations where a similar potency orthosteric modulator fails. This is because allosteric modulators do not compete with the natural ligands, in contrast to orthosteric drugs, as they bind with the receptor on the allosteric site.

Allosteric modulators are highly selective. Receptors comprise multiple functional domains and transmit several message signals to the cell. While an orthosteric drug competes with the natural

ligand for it's highly conserved binding site, allosteric modulators use a different binding site, the allosteric site, which has not been subjected to conservatory evolutionary pressure. Therefore, allosteric modulators are found to be highly selective for one receptor of interest, and thus have the potential to have an increased safety profile compared to other drugs.

Since allosteric modulators bind to the receptor at a site other than the active site, the natural biological rhythm is preserved, which is usually lost/altered in the case of orthosteric modulators.

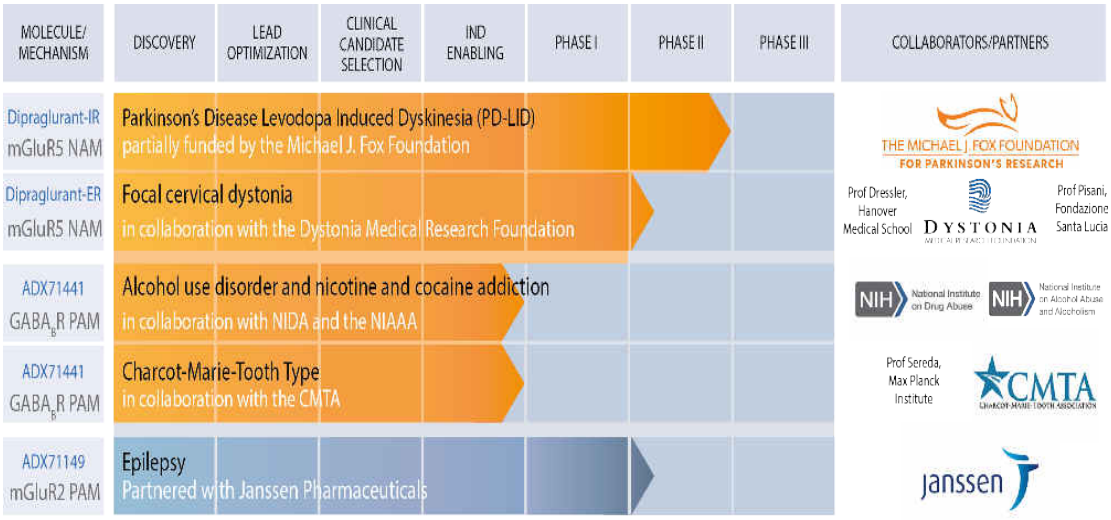
Addex has developed proprietary screening systems to identify allosteric modulators that modify the molecular response of the therapeutic target. These systems screen G-Protein Coupled Receptors (GPCR) and non-GPCR drug targets, and provide the pharmacological data that allow lead optimisation through medicinal chemistry. The company has patented several aspects of these technologies while keeping certain others as trade secrets to maintain its competitive advantage.

Business Strategy & Partnerships

Addex' current business strategy includes the possibility of entering into collaborative arrangements with third parties to complete the development and commercialization of its proprietary drug candidates, such as the current partnership with Janssen Pharmaceuticals, Inc. ("Janssen"), a subsidiary of Johnson & Johnson, for ADX71149 in the treatment of epilepsy and other undisclosed CNS disorders. Addex also received a grant from The Michael J. Fox Foundation for Parkinson's Research for the development of dipraglurant (ADX48621) in the treatment of PD-LID and from the Swiss Commission for Technology and Innovation (CTI) to develop allosteric modulator therapeutics for neurodegenerative and psychiatric diseases. Addex has recently entered a collaboration arrangement with Pierre Fabre Pharmaceuticals to identify mGluR3 allosteric modulators for CNS disorders.

Pipeline: Focus on CNS related indications

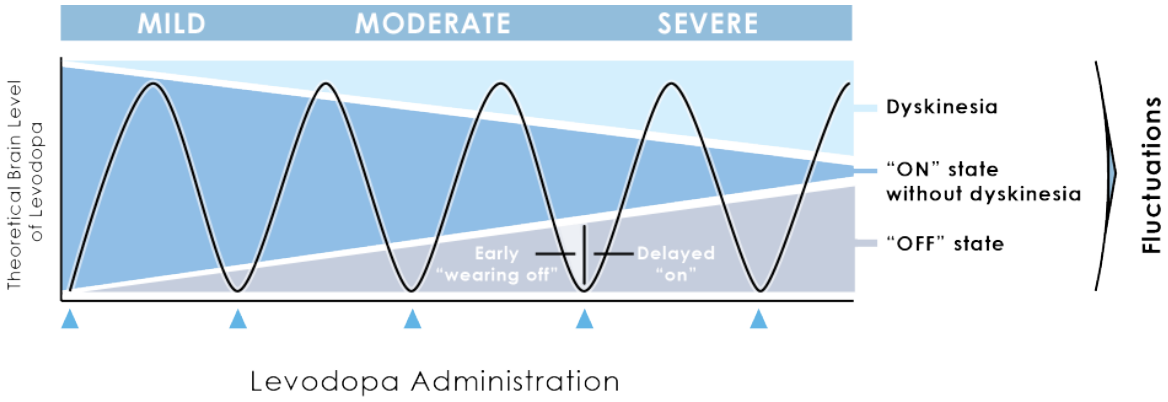
Using its allosteric modulator discovery capabilities, Addex has developed a pipeline of proprietary clinical and preclinical stage drug candidates. In 2012, the company revised its business strategy to focus on the advancement of allosteric modulators of four receptors, namely the metabotropic glutamate receptor 5 (mGlu5), the metabotropic glutamate receptor 2 (mGlu2), the gamma-aminobutyric acid subtype B receptor (GABAb) and the metabotropic glutamate receptor 4 (mGlu4).

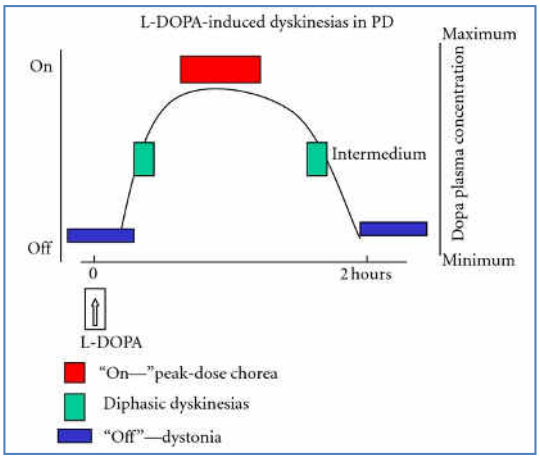


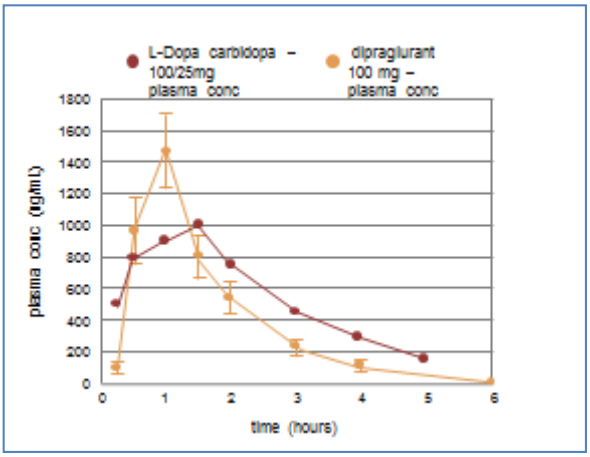
Addex' lead product in development is Dipraglurant IR (immediate release). Dipraglurant is an oral small molecule, which inhibits the metabotropic glutamate receptor 5 (mGluR5), and has potential to be used in combination with levodopa or dopamine agonists for treatment of Parkinson's disease (PD). The company is primarily testing dipraglurant for the treatment of PD levodopa-induced dyskinesia (PD-LID). In a double-blind, placebo-controlled, US and European Phase II study in PD-LID, data showed that dipraglurant met the primary objective of the study by

exhibiting a good safety and tolerability profile. Dipraglurant also demonstrated a statistically significant reduction in LID severity with both 50 and 100 mg doses. Dipraglurant reduced dystonia severity in addition to chorea, the two major LID components. The trial was supported by a grant from The Michael J. Fox Foundation for Parkinson's Research. Dipraglurant has received FDA orphan drug designation for levodopa-induced dyskinesia associated with Parkinson's disease and is currently in preparation to enter a phase III pivotal clinical trial that is expected to commence beginning of 2017.

Addex has specifically developed an immediate release (IR) formulation of dipraglurant that mimics the uptake of levodopa in patients, since peak-dose dyskinesia is the most frequent levodopa-induced dyskinesia. Levodopa has to be given 3-4 times a day due to its relatively short half-life. Peak plasma concentrations are reached 60 to 90 minutes after dosing, when peak-dose dyskinesia occurs. Dipraglurant IR, which is taken together with levodopa, has a rapid onset of action similar to levodopa, and rapid clearance that reduces unnecessary drug exposure and unwanted side effects. This profile is ideal to offset unwanted peak-dose dyskinesia.







The immediate release (IR) formulation is ideally suited for acute treatment of PDLID because:

- Its pharmacokinetic profile is similar to levodopa so drug is delivered precisely when needed.
- Its rapid onset of action is ideal for dyskinesia which can occur within 30 minutes of dosing.
- The rapid clearance reduces unnecessary drug exposure, between levodopa doses and should reduce side effects as a result.
- The PK characteristics of dipraglurant IR have potential to give flexibility of use, which is common practice and desirable in PD treatment

The combined peak US annual sales potential (excluding disease modification) for the PD indications alone is estimated to be in the range of USD 1.8 billion to USD 2.7 billion , (source: Michael J Fox Foundation). Datamonitor market research with PD specialists in the US, EU, China and India show that dipraglurant has an attractive product profile and can capture over USD 1 billion in annual revenues if fully exploited in PD indications.

Parkinson's Disease and Levodopa Induced Dyskinesia

Parkinson's disease is a central nervous system disease, which affects a patient's motor skills, speech and other functions. There is a collection of nerve cells in the brain that control the movements of the body. These nerve cells are called basal ganglia and produce a chemical called dopamine, which sends signals to coordinate the body movement. When around 80% of these dopamine-producing cells die or are damaged, signs of Parkinson's can be observed. Researchers have been unable to identify the causes for a drop in the level of dopamine in these nerve cells.

While there is no cure for Parkinson's disease, medication and surgery can offer substantial relief from the symptoms. All of the current medications are aimed at increasing the level of dopamine in the brain, by replacing it, mimicking it or delaying its breakdown to extend its effect.

Levodopa is the most common medication for Parkinson's disease. It enables the nerve cells to generate dopamine and replenishes the brain's dwindling supply. However, there are various side effects such as nausea, vomiting, low blood pressure, muscle spasms and drowsiness. Moreover, as the disease progresses, the duration of relief from the medication shortens. The patient starts suffering from "end of dose deterioration" or the "wearing off phenomena" and often switches from the "on" state to the "off" state. This demands an increase in the drug dosage that can lead to levodopa-induced dyskinesia or LID.

LID leads to involuntary movements such as twitching, twisting, and writhing. Research indicates that half of the patients develop LID during the first five years of treatment. Chorea and dystonia are the two main components of LID. Chorea is characterized by sudden rapid uncontrollable movements that occur when dopamine derived from levodopa is at its peak in the brain and dystonia is characterised by slow writhing movements and muscle contractions, which occur during the dosage cycle.

In the US, there are an estimated 500,000 to 1 million patients suffering from Parkinson's disease. There are no approved treatment options for PD-LID. Approximately 50% of PD patients will experience LID after 4 to 6 years on L-DOPA therapy. The number rises to 90% after 10 to 15 years on L-DOPA therapy. It is a significant problem for patients and physicians seeking treatment for PD. In fact, a survey of key opinion leaders (KOLs) in the Parkinson's treatment space showed that dyskinesia is the most important unmet medical need in the treatment of PD after a disease modifying agent (Datamonitor 2011). Currently, the most common treatment for LID is to reduce dose on L-DOPA. However, reducing dose on L-DOPA causes increased parkinsonism and worsening motor performance. Therefore, once established, LID becomes difficult to treat.

Near Term Milestones

In the coming 12 months we expect a number of important mile stones that can drive the stock price upwards. These are:

- Dipraglurant pilot study in focal cervical dystonia (Dressler) – start dosing: **2016Q3**
- ADX71441 preclinical data from NIDA collaboration in cocaine addiction: **2016Q2**
- Dipraglurant receptor occupancy study in healthy subjects – full results: Announced
- Dipraglurant Phase II POC study in focal cervical dystonia – start dosing: **2016Q3**
- ADX71441 Phase I – start dosing: **2016Q4**
- ADX71441 Phase I – results: **2017H2**
- Dipraglurant Phase II POC study in focal cervical dystonia – results: **2017H2**
- ADX71441 Phase II POC in CMT1a – start dosing: **2017H2**
- Dipraglurant Phase III study in PD-LID – start dosing: **2017H2**

Analyst: Marcel Wijma MSc

Marcel Wijma, Chief Research Officer and managing partner, has a longstanding history in financial biotech research. After selling Van Leeuwenhoeck Research (VLR) to SNS Securities in 2006, he established an award winning analyst team in biotech/life sciences at SNS Securities. In 2009, Marcel was awarded by Financial Times/Starmine as being one of the Top-3 biotech analysts in Europe. Later that year, Marcel purchased VLR from SNS Securities after which the company was reconstituted. At VLR, he leads the professional VLR research organisation, which is augmented by selected external financial researchers with a specialisation in Life Sciences. Mr. Wijma has a Masters degree in Financial Economics from Erasmus University in Rotterdam.