



Research Note

## Addex Therapeutics

Partnership in Addiction, Valuation Increased



Chief Research Analyst

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<b>Name:</b>	<b>Addex Therapeutics</b>
<b>Country:</b>	<b>Switzerland</b>
<b>Price:</b>	<b>CHF 3.12</b>
<b>ISIN Code:</b>	<b>CH0029850754</b>
<b>Reuters Code:</b>	<b>ADXN.SW</b>
<b>Market Cap (CHF m):</b>	<b>48.0</b>
<b>EV (CHF m):</b>	<b>39.6</b>
<b>Cash &amp; cash eq. (CHF m):</b>	<b>8.6*</b>
<b>Shares outstanding (m):</b>	<b>15.4</b>
<b>Volume:</b>	<b>100,387</b>
<b>Free float:</b>	<b>87%</b>
<b>52-week Range:</b>	<b>1.98-4.00</b>
*) Including payment Indivior partnership	

	<b>2014A</b>	<b>2015A</b>	<b>2016A</b>
<b>Total Revenues</b>	1.03	0.79	0.40
<b>Net (Loss)/Profit</b>	(1.77)	(4.20)	(3.10)
<b>Net loss per share (cents)</b>	(0.18)	(0.39)	(0.28)
<b>R&amp;D costs</b>	0.9	1.78	2.40
<b>Cash increase/(decrease)</b>	(0.95)	0.70	(1.23)
<b>Cash and marketable sec.</b>	1.98	2.63	1.40



### *Addex Therapeutics Signs Partnership in Addiction with Indivior*

Earlier this year, Addex Therapeutics announced a strategic partnership with Indivior PLC for the global development and commercialization of its program ADX71441 for the treatment of addiction. Under the terms of the agreement, Addex will receive USD 5 million upfront, USD 4 million of committed research funding over the next two years, USD 330 million of potential development, regulatory and commercialization milestones and tiered royalties up to double-digit. Addex retains the right to select compounds from the research collaboration for certain indications outside addiction, including Charcot-Marie-Tooth type 1a neuropathy (CMT1A).

Indivior PLC (LON:INDV) is a specialty pharmaceutical company focused on addiction treatment. The company was incorporated in September 2014 as a result of demerger of Reckitt Benckiser Pharmaceuticals Inc from RB Group. Indivior is focused on advancing its therapeutic pipeline to address the growing health epidemic of addiction and related mental health disorders. Indivior’s product pipeline includes: RBP-6000, a buprenorphine 1 month depot in Atrigel® indicated for the treatment of opioid dependence; RBP-6300, a buprenorphine hemiadipate oral swallowable tablet with abuse-deterrent properties indicated for the treatment of opioid dependence; RBP-8000, a cocaine esterase indicated for the treatment of cocaine intoxication. This product has concluded a Phase II trial. No results were made public.

### *Clinical Stage Pipeline Addex Therapeutics*

Molecule / MoA	Preclinical	Phase 1	Phase 2	Phase 3 Pivotal
Dipraglurant-IR (mGluR5 NAM)	Parkinson’s disease levodopa-induced dyskinesia			
Dipraglurant-ER (mGluR5 NAM)	Focal cervical dystonia			
ADX71441 (GABAB PAM)	Addiction			INDIVIOR
(GABAB PAM)	CMT 1A neuropathy			
ADX71149 (mGluR2 PAM)	Epilepsy			Janssen



Source: Addex Therapeutics



### *Partnership Leads to Substantial Higher Valuation*

Our valuation model on Addex Therapeutics shows a value of CHF 179 million or CHF 11.50 per share. In that model, we did address value to the preclinical programs in Addex' pipeline, including its ADX71441 programs. Following the deal with Indivior, this program already has a potential value of at least USD 330 million, taking into account the future milestones and up to double digit royalties. When taking into account a LOA for this program of 15% and peak sales of USD 600-700 million, the risk adjusted NPV of the program would be value at CHF 25-35 million or CHF 1.60-2.30 per share.

### *GABAB PAM: Addiction and Charcot-Marie-Tooth Type 1A*

ADX71441 (GABAB PAM) is the third program drug in Addex' proprietary allosteric modulation technology platform and is targeted for the treatment of addiction (alcohol use disorder, cocaine and nicotine addiction) and has been licensed to Indivior PLC. Researchers have shown that GABAB receptor agonists such as baclofen are effective in reducing drug self-administration, cravings, and anxiety, and thus promote abstinence. Baclofen, also known as chlorophenibut, is a conventional (orthosteric) stimulator (agonist) of the GABAB receptor and is primarily used to treat spasticity and is in early development for treating alcoholism.

GABAB PAM is a fourth program targeted for the treatment of Charcot-Marie-Tooth (CMT) disease. CMT type 1A encompasses a heterogeneous group of inherited, progressive, chronic peripheral neuropathies. The most common type of CMT, is an orphan disease affecting at least 125,000 people in Europe and the U.S. The genetic mutation responsible for CMT1A is a duplication of the PMP22 gene coding for a peripheral myelin protein. Overexpression of this gene causes degradation of the neuronal sheath (myelin) responsible for nerve dysfunction, followed by loss of nerve conduction. As a result of peripheral nerve degradation, patients suffer from progressive muscle atrophy of legs and arms causing walking, running, balance problems and abnormal hand functioning. CMT1A patients end up in wheelchairs in at least 5% of cases. They might also suffer from mild to moderate sensitive disorders. First symptoms usually appear during adolescence and will progressively evolve through patients' life.



In July 2016, Addex published that ADX71441 demonstrated positive results in a highly translational preclinical model of spasticity. ADX71441 was evaluated in a leading model of muscle spasticity, the rat transection spinal cord injury (SCI) model. Muscle hyperactivity was measured by a translational electrophysiological marker, the rate- dependent depression of the Hoffmann's reflex (H-reflex), a measurement that is also used to evaluate spasticity in patients. The SCI procedure significantly induced spasticity in rats within 5 weeks ( $P < 0.001$ ; Mann-Whitney test), after which a single intravenous administration of ADX71441 (1, 3 or 10 mg/kg) or vehicle was administered and the degree of spasticity response was measured.

In preclinical studies, Addex has demonstrated the efficacy of ADX71441 in animal models of alcohol use disorder and nicotine withdrawal. In particular, the Company has conducted three preclinical alcohol use studies in collaboration with the National Institute on Alcohol Abuse and Alcoholism (NIAAA). The Company also recently announced positive results from a study evaluating ADX71441 in a primate model of cocaine addiction, which was conducted in collaboration with the National Institute of Drug Abuse (NIDA). In rhesus monkeys, pre-treatment with ADX71441 dose-dependently reduced cocaine self-administration to roughly 10% of control values. This effect was observed without any concomitant effect on food intake, suggesting that ADX71441 is not broadly affecting the reward circuitry in the brain. Addex plans to launch a Phase I study comparing the safety and efficacy of ADX71441 to baclofen. Baclofen is approved for the treatment of spasticity in the US, but not alcohol use disorder (AUD), despite receiving a temporary registration in France for AUD.

In October the US National Institute on Drug Abuse (NIDA, a division of National Institutes of Health (NIH)) has awarded a USD 5.3 million grant to support human studies of ADX71441 for the treatment of cocaine use disorder. The grant was issued as part of the Grand Opportunity in Medications Development for Substance-Use Disorders (U01), a cooperative agreement providing for both financial assistance and significant scientific support from the NIH to selected clinical



programs. The human studies of ADX71441 will be conducted in coordination with the Friends Research Institute (FRI) and principal investigator, Dr. Frank J. Vocci. The studies are expected to begin in 2018H1.

### *Near Term Milestones*

In the past 12 months, Addex has already reached a number of important milestones that brought the company back on track towards commercialization of its lead candidate. In the coming 12 months, we expect a number of important milestones that can drive the stock price upwards. These are:

- ADX71441 Phase I – start dosing: 2018H2
- Dipraglurant Phase IIa POC study in focal cervical dystonia – start dosing: 2018H1
- ADX71441 Phase I – results: 2019H1
- Dipraglurant first pivotal study in LID registration program – start dosing: 2018H2
- Dipraglurant Phase II POC study in focal cervical dystonia – results: 2019H1
- Dipraglurant first pivotal study in LID registration program – results: 2020H1
- Dipraglurant second pivotal study in LID registration program – start dosing: 2020H1
- Dipraglurant second pivotal study in LID registration program – results: 2021H2



*Analyst: Marcel Wijma MSc*

*Marcel Wijma, Chief Research Officer and managing partner, has a longstanding history in financial biotech research. After selling Van Leeuwenhoek 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.*

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