Update Report

Addex Therapeutics

Janssen moving into Epilepsy Phase 2 Study

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Date: 20 July 2020

Name:	**Addex Therapeutics**
Country:	**Switzerland**
Price:	**CHF 1.40**
ISIN Code:	**CH0029850754**
Reuters Code:	**ADXN.SW, ADXN**
Market Cap (CHF m):	**45.9**
EV (CHF m):	**18.8**
Cash & cash eq. (CHF m):	**27.1**
Shares outstanding (m):	**32.8**
Volume:	**34,643**
Free float:	**63%**
52-week Range:	**0.95-2.41**

	2018A	2019A	2020E
Total Revenues	6.70	2.83	3.50
Net (Loss)/Profit	(1.65	(14.78)	(12.50)
Net loss per share (cents)	(0.07)	(0.56)	(0.38)
R&D costs	4.90	12.45	14.00
Cash increase/(decrease)	39.08	(9.99)	(11.54)
Cash and marketable sec.	41.67	31.54	20.00

Executive Summary

- Addex Therapeutics is a clinical-stage pharmaceutical company focused on the development of an innovative class of oral therapies for neurological disorders. Addex' lead program is ready to start a Phase IIb/III pivotal registration study for levodopa-induced dyskinesia associated with Parkinson's disease (PD-LID) and was scheduled to start in 2020Q1 until initiation was suspended due to the COVID-19 global pandemic. Addex expects to start in 2020H2 with topline data read-out expected in 2022Q2. The potential market for PD-LID drugs has increased substantially following the substantial prices of PD therapeutics. Drugs like Nuplazid and Gocovri were initially priced at USD 30,000 and USD 28,500 per year, respectively. That would value the US PD-LID market at USD 4.2 billion. Should dipraglurant achieve regulatory approval in the US, it is estimated to reach US peak sales of USD 1-1.5 billion potentially.

- In June, the Company announced that program ADX71149 will advance into a Phase 2a proof of concept study in patients with epilepsy. The multi-center study is scheduled to begin dosing patients in the United States early 2021. Janssen Pharmaceuticals, Inc., part of Johnson & Johnson, is responsible for the clinical development and commercialization of this program under the terms of a licensing agreement with Addex. Under the research collaboration and license agreement, Addex granted Janssen an exclusive worldwide license to develop and commercialize mGlu2 PAM compounds. Addex is eligible for up to a total of €109 million in success-based development and regulatory milestone payments. In addition, Addex is eligible for low double-digit royalties on net sales of compounds developed under the agreement.

- Addex now has two active clinical programs with a number of significant value creating milestones ahead, two major collaborations with pharma and a pipeline of earlier-stage programs that are moving rapidly towards the clinic.

- The Company's current cash remains solid and amounts to CHF 27.1 million following a successful raise of CHF 40 million last year and payments from its other pharma partner Indivior. This provides a runway through 2021 and should be sufficient to fund the development of its pipeline and most importantly, substantially through the Phase IIb/III pivotal registration trial with dipraglurant in PD-

LID which is scheduled to start in 2020Q4.

- Based on our NPV based valuation, we believe that Addex remains substantially undervalued at the current share price of CHF 1.40. We believe the share price decrease of the last few months is unjustified and provides a substantial buying opportunity as we expect significant news flow in the coming months as the COVID-19 pandemic diminishes. The announcement of Janssen's decision to advance ADX71149 into a Phase IIa study has a positive effect on the valuation, and we expect the start of both dipraglurant Phase IIb/III pivotal study and ADX71149 Phase IIa Epilepsy study to have a positive impact on the Addex share price. Using our valuation model and taking into account the future revenues from its late-stage clinical pipeline and its current partnerships with Indivior and Janssen, we have increased our valuation to CHF 425-460 million, or CHF 13.00-14.00 per share.

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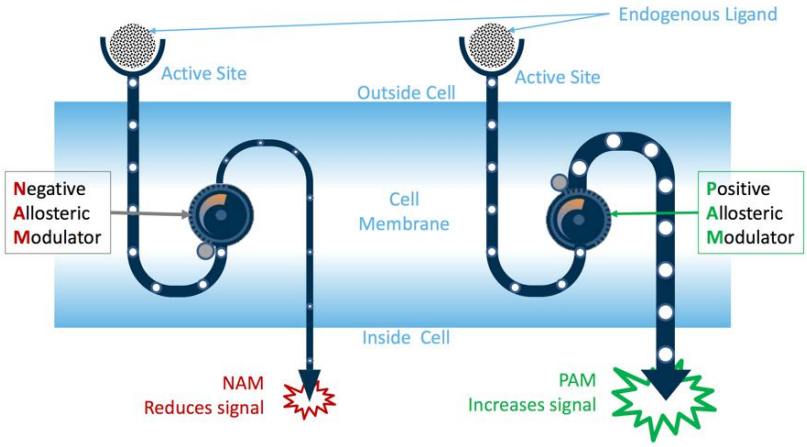
Company Profile

Addex Therapeutics is a clinical-stage pharmaceutical 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.

What are allosteric modulators?

In contrast to competitive compounds, allosteric modulators of GPCRs interact with binding sites that are topographically distinct from the binding site of the endogenous activator, and therefore do not compete with the endogenous activator. This means that allosteric modulators do not activate or inhibit receptors on their own, but only in the presence of an endogenous activator do they enhance (positively modulate) or inhibit (negatively modulate) the natural physiological activity of the receptor. Consequently, allosteric modulators offer the possibility to preserve normal physiological receptor function while controlling pathologic activity caused by over- or under-activation of an endogenous receptor. The below figure shows graphically how an allosteric modulator or a G-protein coupled receptor exercises its activity:



Allosteric modulators potential to unlock undruggable targets

There is an opportunity for an allosteric modulator approach to identify novel orally active compounds for well-validated targets which have no approved drugs because traditional orthosteric approaches have failed to deliver. Developing allosteric modulators for previously undruggable targets is an increasingly exciting space with the vast majority of well understood drug targets currently being undruggable. Allosteric sites are largely unexplored for drug discovery although it is an increasingly hot area. There are a number of proprietary technologies that Addex has developed to identify new allosteric approaches in addition to many years of "know-how" held by the company. Allosteric approaches are also interesting as the IP landscape is less crowded so there may be greater freedom to operate.

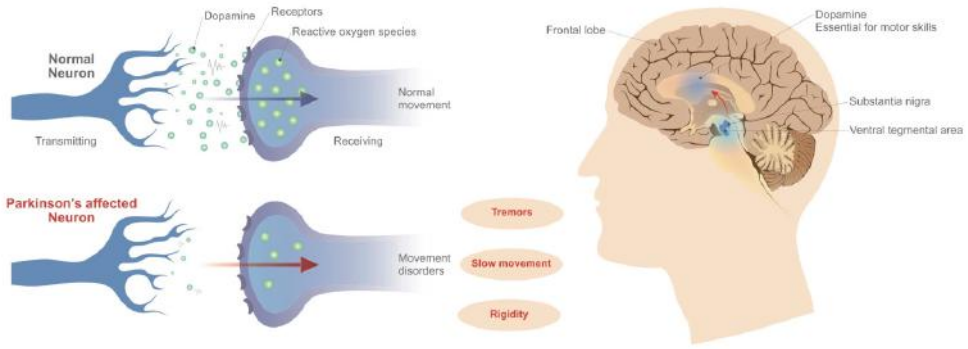
Addex' lead product is dipraglurant that successfully completed a Phase IIa POC trial in Parkinson's disease levodopa induced dyskinesia (PD-LID). The drug is scheduled to start a Phase IIb/III pivotal registration study in PD-LID in 2020H2 with topline data expected in 2022Q2. The potential market for PD-LID drugs has increased substantially following the recent prices of PD therapeutics such as Nuplazid and Gocovri which were initially priced at USD 30,000 and USD 28,500 per year respectively. Based on these prices, the US PD-LID market is estimated at USD 4.2 billion. Should dipraglurant achieve regulatory approval in the US, it is estimated to potentially reach US peak sales of USD 1-1.5 billion.

Dipraglurant: Potentially First-in-Class for Levodopa Induced Dyskinesia associated with Parkinson's Disease

Addex is developing its lead compound, dipraglurant as a novel, orally available negative allosteric modulator (NAM) of the metabotropic glutamate subtype 5 (mGlu5) receptor for the treatment of PD-LID. Addex expects to start a placebo-controlled Phase IIb/III pivotal registration clinical trial of dipraglurant for PD-LID in 2020H2, subject to COVID-19 restrictions being lifted in the United States. Topline results are expected in 2022Q2. This is approximately 9 months later that previously announced due to the COVID-19 coronavirus pandemic. The study will be conducted in the United States and will target enrollment of approximately 140 patients. Addex has received orphan drug designation from the United States Food and Drug Administration (FDA) for dipraglurant in PD-LID.

Parkinson's disease and levodopa induced dyskinesia

Parkinson's disease (PD) is a neurodegenerative brain disorder that results from the death of dopamine-generating cells in the substantia nigra region of the midbrain. PD is also characterized by the accumulation of a protein called alpha-synuclein into inclusions called Lewy bodies in neurons. The cause of PD is generally idiopathic, although some atypical cases have a genetic origin and certain environmental factors are known to play a role. There are approximately 1,000,000 patients with Parkinson disease in the US, with 50,000 to 60,000 more diagnosed each year. Worldwide, there are approximately 4 million individuals afflicted (2.7 million in the US, Japan, and the 5 major European markets). Since the incidence of PD increases with age (the average age of onset is 60), the number of patients is likely to climb as the population of older patients grows.



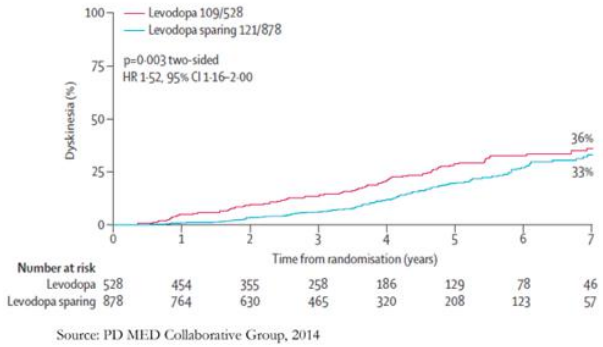
There is no cure for PD. Instead, physicians attempt to manage the symptoms of the disease through a multidisciplinary approach that may include pharmacological, social, and surgical options. The most common pharmaceutical treatment options are those which look to increase the level of dopamine in the brain. These include dopamine replacement therapies (DRT) combined with dopa decarboxylase inhibitors, dopamine agonists, and MAO-B inhibitors.

The most commonly used DRT therapy is Levodopa which has been available for over 30 years and is the mainstay of therapy. Levodopa is converted into dopamine in the dopaminergic neurons by dopa decarboxylase. The administration of levodopa temporarily diminishes the motor symptoms associated with the lack of dopamine in the substantia nigra. Unfortunately, only about 5-10% of Levodopa crosses the blood-brain barrier with the remainder being metabolized to dopamine elsewhere. PD patients experience a variety of side effects including nausea, dyskinesias and joint stiffness. As a result, despite its effectiveness in reducing motor symptoms associated with Parkinson's disease, physicians often attempt to delay Levodopa therapy until the disease progresses to a more moderate-to-severe stage. Most early stage PD patients start out on MAO-B inhibitors and/or dopamine agonists, or low-dose Levodopa. However, PD is a progressive and degenerative disease, and patients typically progress to the point where starting Levodopa or increasing the Levodopa dose is necessary within five years of the initial diagnosis. After a decade on therapy, almost all PD patients require high doses of Levodopa, as well as surgical options including deep brain stimulation (DBS). As the dose and use of Levodopa increases, the incidence of dyskinesia also increases. Levodopa also has a relatively short half-life, requiring dosing between three to four times a day and as high as 8 times a day for late stage patients. Peak plasma

concentrations of Levodopa occur 60 to 90 minutes after dosing. Unfortunately, this is also when peak side effects such as dyskinesia occur. The hefty dosing requirement of Levodopa creates compliance issues, especially at night when patients may sleep through their dose schedule – dosing every six hours. The peaks and troughs associated with Levodopa create significant "on" and "off" treatment times for PD patients. On times are when the drug is in their system and they may be experiencing dyskinesia, and off times are when the Levodopa has left their system and the patient may awake in a frozen or rigid state.

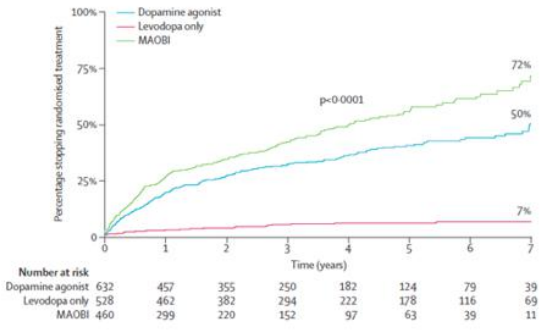
Despite the occurrence of Levodopa Induced Dyskinesia, Levodopa remains the mainstay in PD treatment. In a large clinical study that was done in 2000-2009 in the UK, 1620 patients were randomized to receive Levodopa, dopamine agonists and MAO-B inhibitors. The patients were followed for 7 years to get their responses to the drugs. It showed that patients who were treated with levodopa sparing approaches, had similar rates of dyskinesia over time to those treated with levodopa. However, the study showed that the rate of discontinuations were considerably lower in the patient group using Levodopa (7% discontinuations) compared to 72% for MAO-B inhibitors and 50% for dopamine agonists. This validated Levodopa as the gold standard in PD treatment (see graphs below)

Comparison of Dyskinesia Rates



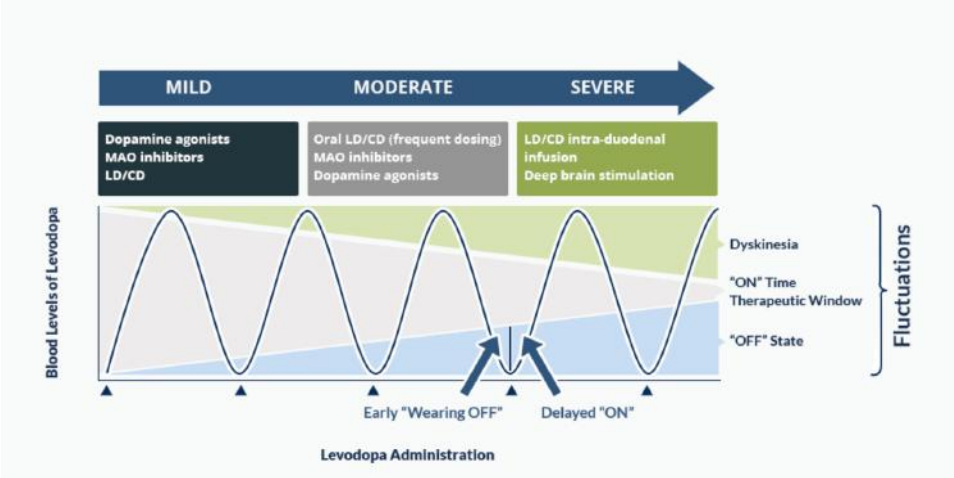
Source: PD MED Collaborative Group, 2014

Comparison of Discontinuations



Long-term Levodopa use is invariably associated with the development of dyskinesias that becomes as disabling as the PD symptoms themselves. Dyskinesia results from the

neurodegenerative process that underlies PD. The dopamine replacement does not lead to dyskinesia per se but is thought to lower the triggering threshold for symptoms, as the neurodegeneration progresses. Dyskinesia is characterized by hyperkinetic movements, including chorea (abnormal involuntary movement), dystonia (sustained muscle contraction, abnormal posture), and athetosis (involuntary convoluted movements). It is most common at times of peak Levodopa plasma concentrations (peak-dose dyskinesia), although it may also occur when plasma concentrations of Levodopa rise and fall (diphasic dyskinesia) or during off-time (off-period dystonia). The following figure shows the evolution of Parkinson's disease, treatment options and the development of dyskinesia as the disease progresses.



Approximately 50% of PD patients will experience dyskinesia after 3 years on Levodopa therapy. The number rises to 90% after 9 to 15 years on Levodopa 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). Although the first treatment for Dyskinesia associated with PD was approved by the FDA in 2017 (Gocovri from Adamas Pharmaceuticals), the most common treatment for Dyskinesia is to reduce the dose of Levodopa. However, reducing the dose of Levodopa causes increased parkinsonism and worsening motor performance. Therefore, once established, Dyskinesia becomes difficult to treat.

Pipeline: Turning into late stage CNS play

Using its allosteric modulator discovery capabilities, Addex has developed an extensive pipeline of proprietary clinical and preclinical stage drug candidates. Addex allosteric modulator discovery platform is broadly applicable and can be applied to the discovery of small molecule allosteric modulators for any protein target. However, Addex has focused its efforts on metabotopic glutamate receptors and gamma aminobutyric acid subtype B receptor (GABAb) for CNS disorders which are a lower risk approach due to the extensive clinical validation of the receptor classes. Also, mGlu5NAM proved to be a strongly validated target for PD-LID following new insight on Novartis' mavoglurant data, in addition to the Addex Dipraglurant Phase IIa data. Glutamate is the main excitatory neurotransmitter in the central nervous system, which includes the brain and the spinal cord, participating in a wide range of neural functions such as learning and memory. With Janssen progressing the Epilepsy program into Phase II, the company has another molecule in mid stage clinical development.

Addex' extensive clinical and late preclinical portfolio is as follows:

Molecule / MoA	Indication	Partner	Pre-clinical	Phase 1	Phase 2	Phase 3	Milestone
Dipraglurant-IR (mGlu5 NAM)	PD-LID						Expect topline results in Q2 2022
Dipraglurant-ER (mGlu5 NAM)	Dystonia						
ADX71149 (mGlu2 PAM)	Epilepsy	janssen					Expect topline results in Q1 2022
$GABA_B$ PAM	Addiction	INDIVIOR					
	CMT1A						
mGlu7 NAM	Post-traumatic stress disorder	eurostars					
mGlu2 NAM	Mild neurocognitive disorders						
mGlu4 PAM	Parkinson's disease						
mGlu3 PAM	Neurodegenerative disorders						

Source: Addex Therapeutics

Dipraglurant IR for PD-LID

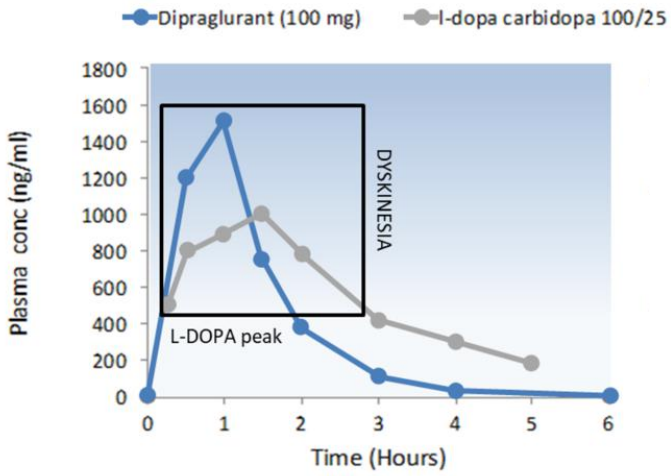
Addex lead program, dipraglurant for Dyskinesia associated with Parkinson's disease (PD-LID) has seen a dramatic increase in its market potential due to increased pricing, a clearer view on the number of patients and receipt of orphan drug designation from the FDA. The program has patent protection through 2034 without extensions. In addition, orphan drug status provides 7 years market exclusivity in the US from the date of launch. Dipraglurant is a highly selective oral small molecule, which inhibits the metabotropic glutamate receptor 5 (mGlu5) and has potential to be used in combination with levodopa or dopamine agonists for treatment of PD-LID. The potential market for PD-LID drugs has increased substantially following the significant price increases of PD therapeutics. Drugs like Nuplazid and Gocovri were initially priced at USD 30,000 and USD 28,500 per year respectively. That would value the US LID market at USD 4.2 billion. Dipraglurant is estimated to reach US peak sales of USD 1-1.5 billion.

Unique Pharmacokinetic profile of Dipraglurant

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 and in severe cases up to 8 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 PD-LID because:

- Its pharmacokinetic profile is similar to levodopa so drug is delivered 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

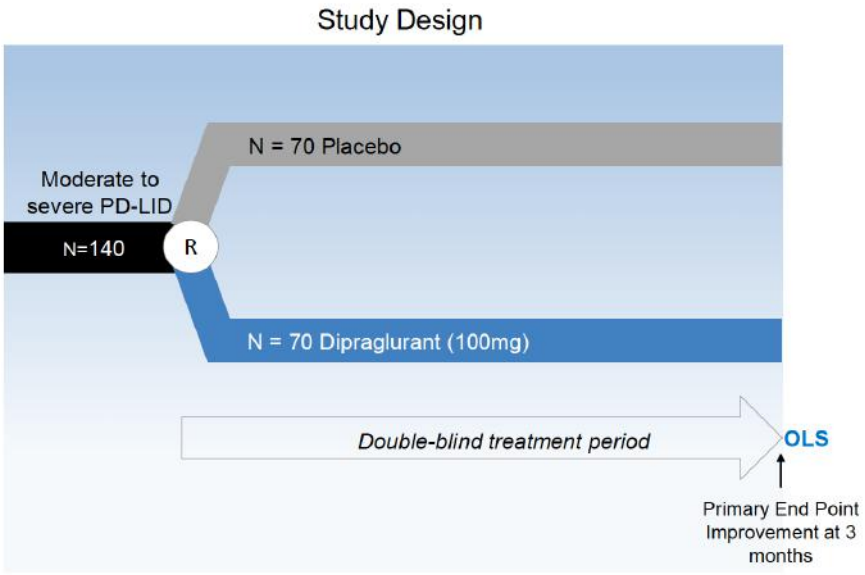


Upcoming Phase IIb/III study Dipraglurant

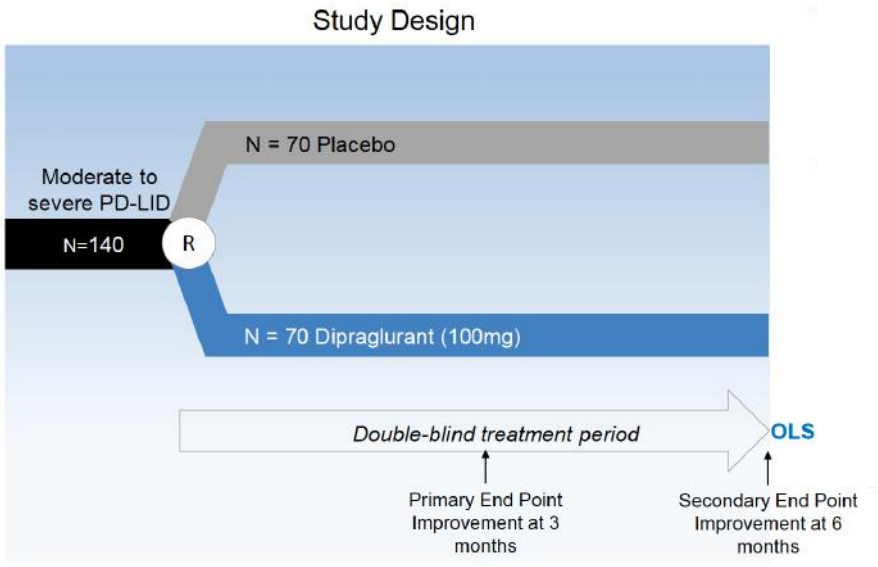
The company has launched a pivotal development program to support regulatory filing of dipraglurant in PD-LID with the first pivotal clinical trial starting in 2020H2. This randomized, double blind, placebo-controlled Phase IIb/III pivotal registration study will assess the safety and efficacy of dipraglurant for the treatment of 140 patients with moderate to severe levodopa induced dyskinesia. Patients will be randomized 1:1 to receive dipraglurant or placebo three times daily, with three of their levodopa doses over a 3 month period. Patients' levodopa treatment regimens will remain consistent over the study. The primary endpoint is change over time in Unified Dyskinesia Rating Scale (UDysRS) at 3 months. This is important as the expectation is that UDysRS is both a more sensitive scale and less prone to placebo effect compared to the mAIMS, and consequently we expect the change in the scale to be in favor of demonstrating efficacy. In addition, UDysRS is the recommended scale of the Movement Disorder Society and with the approval of Gocovri by the FDA in 2017, there is a precedent for the use of UDysRS. Furthermore, it contains anchored objective clinician evaluated measures of dyskinesia as well as patient-based perceptions of disability. UDysRS was developed in 2009 specifically for dyskinesia in PD patients, whereas mAIMS was developed in 1970 to assess tardive dyskinesia in psychiatric patients. The

secondary endpoints include change in clinician-scored Unified Parkinson's disease rating scale (UPDRS) Part III, and patient diaries for on and off time.

Dipraglurant 1st Pivotal LID Study (301)



Dipraglurant Confirmatory Phase III PD-LID Study (303)



ADX71149: Epilepsy (partnership with Janssen Pharmaceuticals)

ADX71149 (JNJ-40411813) is a novel, first-in-class, potent, oral, small molecule positive allosteric modulator (PAM) of metabotropic glutamate subtype 2 (mGlu2) receptor, a Family C class of G Protein Coupled Receptor (GPCR). The development of ADX71149 is part of a worldwide license agreement between Addex and Janssen Pharmaceuticals, Inc., (Janssen), part of Johnson & Johnson, to discover, develop and commercialize a novel mGlu2 PAM medication. Under the terms of the agreement, Addex is eligible for up to a total of EUR 112 million in milestone payments based on potential development and regulatory achievements. Remaining milestones amount to EUR 109 million. In addition, Addex is eligible for low double-digit royalties on sales of any mGlu2 PAM medication developed under the agreement. The Company recently announced that ADX71149, will advance into a Phase IIa proof of concept study in patients with epilepsy. The multi-center study is scheduled to begin dosing patients in the United States early 2021. Janssen is responsible for the clinical development and commercialization of ADX71149 under the terms of a licensing agreement with Addex.

Glutamate is the primary excitatory neurotransmitter in the brain and plays a key role in the initiation and spread of seizures. When activated, the mGlu2 receptor decreases the release of glutamate and consequently helps to maintain neurotransmitter balance. In the presence of agonist-induced activation, positive allosteric modulation of mGlu2 receptors could result in the normalization of the excessive glutamate release seen during a seizure.

Epilepsy is one of the most common serious neurological disorders, affecting about 65 million people globally (Thurman et al. 2011). It affects 1% of the population by age 20 and 3% of the population by age 75. Epilepsy describes a condition in which a person has recurrent seizures due to a chronic, underlying process. It also refers to a clinical phenomenon rather than a single disease entity, since there are many forms and causes of epilepsy. Epilepsy is a disease of the brain defined by any of the following conditions:

- at least two unprovoked (or reflex) seizures occurring more than 24 hours apart;
- one unprovoked (or reflex) seizure and a probability of further seizures similar to the general recurrence risk (at least 60%) after two unprovoked seizures, occurring over the next 10 years;
- diagnosis of an epilepsy syndrome.

The synaptic vesicle protein 2A (SV2A) has been identified as a broad spectrum anticonvulsant target in models of partial and generalized epilepsy, and studies in animal models and human tissue suggest that changes in the expression of SV2A are implicated in epilepsy (Mendoza-Torreblanca et al. 2013; Kaminski et al. 2012). SV2A ligands include levetiracetam (Lynch et al. 2004), which is an anti-epileptic drug commercialized under trademark Keppra®, approved in Europe and USA as a monotherapy or add-on therapy in patients diagnosed with epilepsy. In the 6Hz psychomotor seizure test, a preclinical model of epilepsy considered to be the most relevant model of pharmacoresistant limbic seizures, ADX71149 demonstrated efficacy both stand alone and in combination with SV2a ligands including levetiracetam (Metcalf et al. 2017). In particular, the data show that while seizures are reduced when mGlu2-acting compounds are administered alone, their combination with levetiracetam results in a truly synergistic effect and therefore could reduce the dose required to produce full efficacy, which is important because higher doses of levetiracetam are associated with dose-limiting side effects, such as aggression, nervousness/anxiety, somnolence and fatigue. In this study, a fixed dose of ADX71149 was seen to increase the potency of levetiracetam, leading to an approximate 35-fold increase in its potency. Conversely, using a fixed dose of levetiracetam with varying doses of ADX71149 resulted in an approximate 14-fold increase in ADX71149 potency. If this effect can be translated in the clinic, it will strongly support a rational polypharmacy concept in the treatment of epilepsy patients.

The potential market for ADX71149 could be more than a billion USD. Keppra and its longer acting formulation, Briviact are marketed by UCB who reported 2019 sales of EUR 770 million and EUR 220 million for Keppra and Briviact, respectively.

Financials

In 2019FY, Addex generated income of CHF 2.8 million compared to CHF 6.0 million in 2018, primarily due to the absence of the USD 5.0 million (CHF4.8 million) upfront payment received from Indivior in January 2018 but partially offset by the increase in collaborative research funding from Indivior PLC. Research and development expenses increased by CHF7.5 million to CHF 12.4 million in 2019 compared to CHF 4.9 million in 2018, mainly due to an increase in outsourced development costs related to our dipraglurant PD-LID program and to a lesser extent our $GABA_B$ PAM program. G&A expenses increased by CHF 1.8 million to CHF 5.0 million in 2019, compared to CHF 3.2 million in 2018, mainly due to the increase in headcount and costs related to preparing the listing of ADSs representing our shares on the Nasdaq Stock Market. The net loss for 2019 was CHF 14.8 million compared to CHF 1.6 million for 2018. Cash and cash equivalents amounted to CHF 27.1 million at March 31, 2020 compared to CHF 38.9 million at March 31, 2019 and CHF 31.5 million at December 31, 2019.

Profit & Loss Statement

CHF million	2017A	2018A	2019A	2020Q1
Revenues	0.500	6.701	2.832	0.952
R&D Costs	(2.629)	(4.920)	(12.453)	(3.553)
SG&A	(1.106)	(3.209)	(4.894)	(1.673)
Operating Profit/(Loss)	(3.235)	(1.425)	(14.604)	(4.273)
Finance result	(0.045)	(0.220)	(0.176)	(0.033)
Net Profit/(Loss)	(3.280)	(1.645)	(14.783)	(4.306)

Consolidated statement of cash flows

CHF million	2017A	2018A	2019A	2020Q1
Cashflow from operating activities	(2.135)	1.752	(9.482)	(4.160)
Cash flow from investing activities	(0.02)	(0.062)	(0.043)	(0.009)
Cash flow from financing activities	3.355	37.390	(0.464)	(0.210)
Cash and cash equivalents at beginning of the period	1.416	2.579	41.670	31.537
Net change in cash and cash equivalents	1.214	39.080	(9.989)	(4.379)
Cash and cash equivalents at the end of the year	2.579	41.670	31.537	27.126

Valuation and Share Price Performance

Programs are progressing towards higher valuation

Addex now has two active clinical programs with a number of significant value creating milestones ahead, two major collaborations with pharma and a pipeline of earlier-stage programs that are moving rapidly towards the clinic. These factors all justify a considerably higher value than the current share price is showing. We value Addex Therapeutics at **CHF 425-460 million or CHF 13.00-14.00** per share. This valuation is calculated based on three programs: unpartnered lead program, Dipraglurant for PD-LID in Parkinson's, GABAB PAM for addiction with Indivior and ADX71149 for epilepsy with Janssen. At this moment we do not take a value for the Dystonia Program into account as Addex is currently completing preclinical evaluation of dipraglurant in this disease area. See summary of valuation in the table below.

Program	Indication	Partner	Stage	Valuation
Dipraglurant-IR	PD-LID	-	Start Phase IIb/III H2 2020	CHF 345 million
GABAB PAM	Addiction	Indivior	Start Phase I 2022	CHF 50-85 million
ADX71149	Epilepsy	Janssen	Start Phase IIa 01/2021	CHF 28 million

Another measurement for the potential value of Addex Therapeutics, is making a comparison with companies that have programs in development in PD-LID (dipraglurant), Parkinson's and Addiction since we believe these programs to be the most promising. We should note that in the past few years there has been considerable M&A activity in the Parkinson's field. In 2014 Acorda Therapeutics acquired Civitas for USD 525 million in cash in order to get the rights to its PD drug Inbrija. The drug received approval by the FDA in January. Sunovion acquired Cynapsus in 2016 for USD 624 million to get the rights to Cynapsus' Phase III PD candidate APL-130277. Sunovion

filed for approval in March 2018. Last year Israeli company Neuroderm was bought by Mitsubishi Tanabe Pharma for USD 1.1 billion. Neuroderm has three clinical stage product candidates in development for PD. And last but not least, Lundbeck acquired Prexton Therapeutics in a deal worth EUR 905 million and obtained rights to Foliglurax.

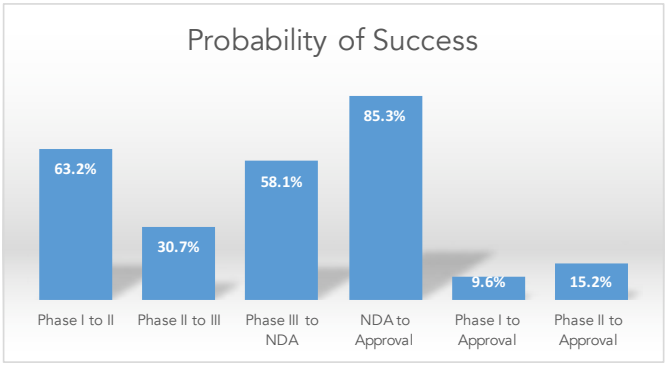
Company	Acquired by	Deal size	Comments
Civitas	Acorda Therap.	USD 525m	FDA granted approval for Inbrija in January 2019
Cynapsus	Sunovion	USD 624m	Acquired Cynapsus and got the rights to PD drug APL130277, currently in Phase III
Neuroderm	Mitsubishi Tanabe Pharma	USD 1.1bn	Lead product is ND0612 for the treatment of PD. Intend to submit regulatory applications for ND0612 in Europe by the end of 2018.
Prexton Therap.	Lundbeck	EUR 905m	Rights to PD drug Foliglurax, currently in Phase II, no clinical efficacy data yet.

Phase Success and Likelihood of Approval (LOA)

In estimating a value for the clinical programs with dipraglurant, we made use of several studies that were done on the clinical development success rates for investigational drugs to measure success rates for investigational drugs. We analyzed individual drug program phase transitions from January 1, 2006 to December 31, 2015. For the ten years studied, 9,985 transitions in the Biomedtracker database were analyzed. A phase transition is the movement out of a clinical phase – for example, advancing from Phase I to Phase II development, or being suspended after completion of Phase I development. These transitions occurred in 7,455 clinical drug development programs, across 1,103 companies (both large and small), making this the largest study of its kind. With this broad set of data, we aimed to capture the diversity in drug development across levels of novelty, molecular modalities, and disease indications. Only company-sponsored, FDA registration-enabling development programs were considered; investigator-sponsored studies were excluded from this analysis.

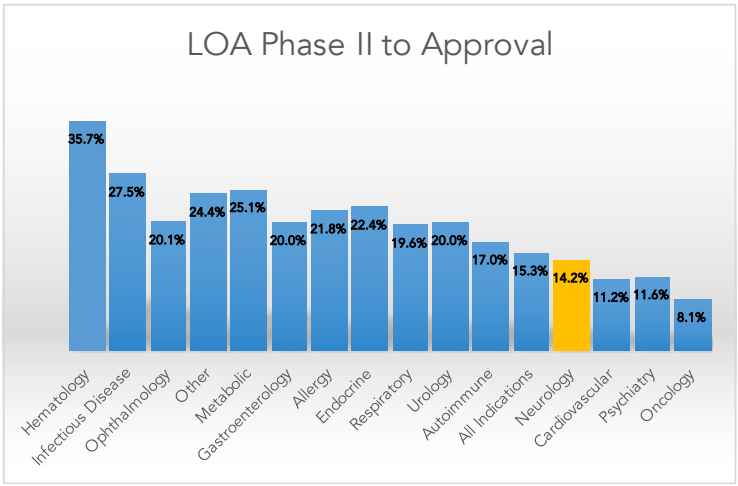
The Phase I transition success rate was 63.2% (n=3,582). As this Phase is typically conducted for safety testing and is not dependent on efficacy results for candidates to advance, it is common for this phase to have the highest success rate among the clinical phases across most categories analyzed in this report. Phase I success rates may also benefit from delayed reporting bias, as some larger companies may not deem failed Phase I programs as material and thereby not report them

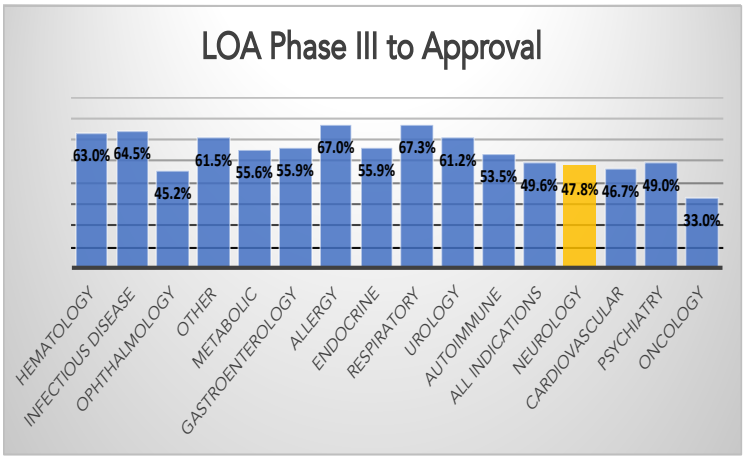
in the public domain. The Phase II transition success rate (30.7%, n=3,862) was substantially lower than Phase I, and the lowest of the four phases studied. As this is generally the first stage where proof-of-concept is deliberately tested in human subjects, Phase II consistently had the lowest success rate of all phases. This is also the point in development where industry must decide whether to pursue the large, expensive Phase III studies and may decide to terminate development for multiple reasons including commercial viability. The second-lowest phase transition success rate was found in Phase III (58.1%, n=1,491). This is significant as most company-sponsored Phase III trials are the longest and most expensive trials to conduct. The probability of FDA approval after submitting a New Drug Application (NDA) or Biologic License Application (BLA), taking into account re-submissions, was 85.3% (n=1,050). Multiplying these individual phase components to obtain the compound probability of progressing from Phase I to U.S. FDA approval (LOA) reveals that only 9.6% (n=9,985) of drug development programs successfully make it to market (see graph below)



Source: BIO Industry Analysis

Major disease areas were segmented according to the convention used by Biomedtracker, and categorized 21 major diseases and 558 indications for the 2006-2015 timeframe. As can be seen in the graphs below, there is a wide range of Likelihood of Approval (LOA) from Phase II and III.





Valuation dipraglurant IR in PD-LID

In estimating a value for dipraglurant in PD-LID, we took into account potential markets in the US and Europe with a total number of potential patients with PD-LID of 180,000 in the US and 225,000 in Europe, with a market launch in the US in 2025 and 2026 in Europe. We calculate a Risk adjusted Discount Rate of 15%. Annual pricing is conservatively set at USD 24,000 for the US and USD 15,000 for Europe which is actually lower than initial pricing of competitive drugs (Gocovri for PD-LID was first priced at USD 28,500, Pimavanserin for PDP was priced initially at USD 24,000 and whereas Igrezza is even priced at USD 60,000-90,000). We notice that pricing of Gocovri is decreasing following the disappointing commercial roll out of the drug. Although we believe that

Addex will potentially partner its program in PD-LID with a large pharmaceutical, in our model we have calculated its value by marketing the drug independently. We estimate that a peak market share of 25-30% is possible. Compared with the report of BioMedTracker (see neurological disorders), we used a higher LOA of 25% as we believe that the vast amount of data justifies that.

This leads to a total valuation for dipraglurant of CHF 345 million or CHF 10.50 per share.

In our view, the delay of the start of the pivotal trail with 6-9 months due to the COVID-19 coronavirus pandemic does not have an impact on our valuation model for the PD-LID program.

Valuation in PD-LID US Market

Year	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	
No of patients US (yoy growth 2.5% as of 2015)	241244	247275	253457	259793	266288	272945	279769	286763	293932	301280	
Penetration	0.5%	1.5%	4.0%	7.0%	11.0%	15.0%	18.0%	21.0%	22.0%	23.0%	
Total Revenues (USD m)	**28.9**	**89.0**	**243.3**	**436.5**	**703.0**	**982.6**	**1208.6**	**1445.3**	**1552.0**	**1663.1**	
Margin 50%	14.5	44.5	121.7	218.2	351.5	491.3	604.3	722.6	776.0	831.5	
WACC 15%	0.50	0.43	0.38	0.33	0.28	0.25	0.21	0.19	0.16	0.14	
NPV (million)	7.2	19.2	45.7	71.3	99.9	121.4	129.9	135.1	126.1	117.5	
Total NPV (million)											**873.5**
LOA 25%											**218.4**

Valuation in PD-LID European Market

Year	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	
No of patients Europe (yoy growth 2.5% as of 2015)	296730	304148	311752	319546	327534	335723	344116	352719	361536	370575	
Penetration	0.5%	1.5%	4.0%	7.0%	11.0%	15.0%	18.0%	21.0%	22.0%	23.0%	
Total Revenues (USD m)	**22.3**	**68.4**	**187.1**	**335.5**	**540.4**	**755.4**	**929.1**	**1111.1**	**1193.1**	**1278.5**	
Margin 50%	11.1	34.2	93.5	167.8	270.2	377.7	464.6	555.5	596.5	639.2	
WACC 15%	0.43	0.38	0.33	0.28	0.25	0.21	0.19	0.16	0.14	0.12	
NPV (million)	4.8	12.9	30.6	47.7	66.8	81.2	86.8	90.3	84.3	78.6	
Total NPV (million)											**505.3**
LOA 25%											**126.3**

Valuation ADX71149 in Epilepsy

With the announcement that Janssen Pharmaceuticals is advancing ADX71149 into a Phase IIa proof of concept study in patients with epilepsy, we decided to include this program into our

valuation model. The multi-center study is scheduled to begin dosing patients in the United States early 2021. We expect that a potential drug can be marketed as of 2025 priced annually at USD 5,000 and a peak market share of 12-15%, which would make this drug a potential block buster for Janssen Pharmaceuticals. Compared with the report of BioMedTracker (see neurological disorders), we used a higher LOA of 20% as we believe that the vast amount of data in other indications as well justifies that.

This leads to a total current valuation for ADX71149 of CHF 28 million or CHF 0.85 per share.

Valuation ADX71149 in Epilepsy

Year	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	
No of patients US (yoy growth 2.5% as of 2015)	1408656	1429786	1451233	1473002	1495097	1517523	1540286	1563390	1586841	1610644	
Penetration	0.5%	1.5%	4.0%	7.0%	11.0%	15.0%	18.0%	21.0%	22.0%	23.0%	
Total Revenues (USD m)	0.5%	1.0%	2.0%	4.0%	8.0%	10.0%	12.0%	13.0%	14.0%	15.0%	
Royalty 12%	$35.2	$71.5	$145.1	$294.6	$598.0	$758.8	$924.2	1,016.2	1,110.8	1,208.0	
WACC 15%	4.2	8.6	17.4	35.4	71.8	91.1	110.9	121.9	133.3	145.0	
NPV (million)	0.62	0.56	0.51	0.47	0.42	0.39	0.35	0.32	0.29	0.26	
Total NPV (million)											**137.3**
LOA 20%											**27.5**

Valuation GABAB PAM in Addiction

Based on the partnership with Indivior, the program in addiction has potential milestones of USD 330 million and tiered royalties up to low double digit. When taking into account likelihood of approval (LOA) for this program of 15% and peak sales of USD 600-700 million, the risk adjusted net present value (NPV) of the program would be CHF 50-85 million or CHF 1.75-3.00 per share.

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.

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