Update Report

Addex Therapeutics

Start of Pivotal Clinical Trial in PD-LID Imminent
Stock Grossly Undervalued

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Name:	**Addex Therapeutics**
Country:	**Switzerland**
Price:	**CHF 1.56**
ISIN Code:	**CH0029850754**
Reuters Code:	**ADXN.SW**
Market Cap (CHF m):	**52.8**
EV (CHF m):	**16.1**
Cash & cash eq. (CHF m):	**36.7**
Shares outstanding (m):	**32.8**
Volume:	**25,492**
Free float:	**63%**
52-week Range:	**1.43-2.52**

	2017A	2018A	2019E
Total Revenues	0.50	6.70	2.50
Net (Loss)/Profit	(3.24)	(1.65)	(12.50)
Net loss per share (cents)	(0.25)	(0.207)	(38.11)
R&D costs	2.46	4.90	10.00
Cash increase/(decrease)	1.22	39.08	(11.67)
Cash and marketable sec.	2.59	41.67	30.00

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 scheduled to start a Phase IIb/III pivotal registration study for levodopa-induced dyskinesia associated with Parkinson's disease (PD-LID) in 2020Q1 with topline data read-out expected in 2021H2. 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 potentially reach US peak sales of USD 1-1.5 billion.

- Addex has a proprietary small molecule allosteric modulator discovery platform which it has used to discover its pipeline of in-house discovered programs including dipraglurant. Allosteric modulators offer several advantages over conventional non-allosteric molecules and may offer an improved therapeutic approach to existing drug treatments. The allosteric space is getting more attention as an increasing number of big pharma players have developed or in-licensed allosteric drugs like and allosteric drugs have made it to commercialization.

- The Company's current cash is very strong and amounts to CHF 36.7 million following a successful raise of CHF 40 million last year and payments from its partner Indivior. This provides a runway through 2021 and should be sufficient to fund the development of its pipeline and most importantly, the completion of the Phase IIb/III pivotal registration trial with dipraglurant in PD-LID in 2020Q1.

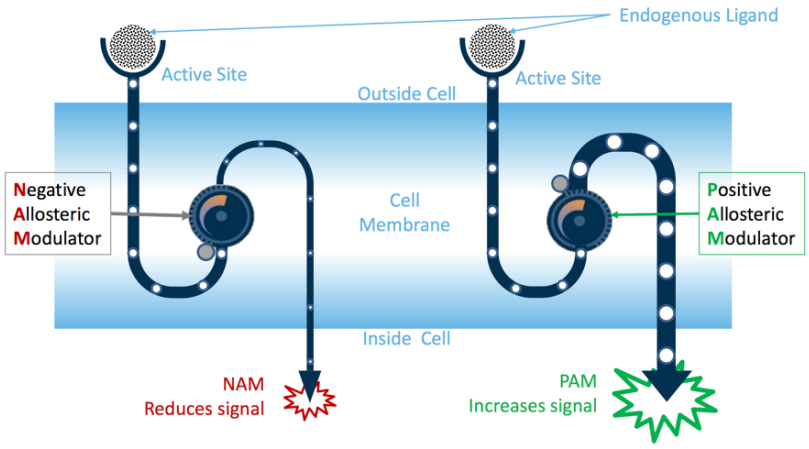
- Based on our NPV based valuation, we believe that Addex remains substantially undervalued at the current share price of CHF 1.61. We believe the share price decrease of the last few months is unjustified and provides a strong buying opportunity as we expect the start of the pivotal clinical trial in PD-LID and the US listing to have a significant impact on the share price next year. Using our valuation model and taking into account the future revenues from its late stage clinical pipeline as well as its current partnership with Indivior, we have increased our valuation to CHF 395-430 million, or CHF 12.00-13.10 per share. This represents a substantial upside from the current share price.

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 2020Q1 with topline data expected in 2021H2. 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.

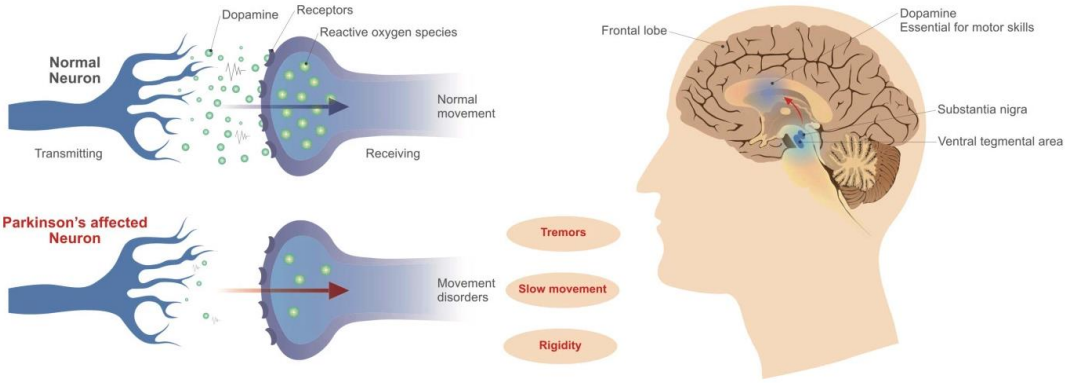
In October, the company announced that Addex' partner Indivior PLC (LON: INDV) will provide the company with an additional USD 800,000 in 2019 to accelerate research progress in their collaboration to develop further oral gamma-aminobutyric acid subtype B (GABAB) positive allosteric modulator (PAM) compounds for the treatment of addiction. Under the terms of the original agreement signed with Indivior in January 2018, Addex received a USD 5 million upfront and a minimum of USD 2 million per year of research funding for 2 years. Under the agreement, Addex is eligible for USD 330 million in milestone payments and tiered royalties up to double digit.

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 receptor subtype 5 ("mGluR5) 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 2020Q1 with topline results expected in 2012H2. 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. 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.



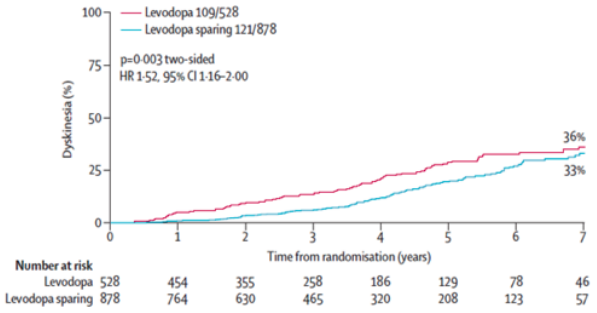
There is no cure for PD. Instead, physicians attempt to manage the symptoms of the disease through a multidisciplinary approach that may include pharmacological, social, and surgical options. The most common pharmaceutical treatment options are those which look to increase the level of dopamine in the

brain. These include dopamine replacement therapies (DRT) combined with dopa decarboxylase inhibitors, dopamine agonists, and MAO-B inhibitors.

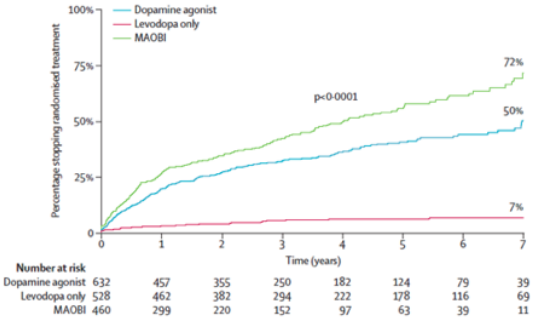
The most commonly used DRT therapy is Levodopa. It has been available for over 30 years. Levodopa (L-DOPA) is converted into dopamine in the dopaminergic neurons by dopa decarboxylase. The administration of levodopa temporarily diminishes the motor symptoms associated with the lack dopamine in the substantia nigra. Unfortunately, only about 5-10% of LDOPA crosses the blood-brain barrier. The remainder is often metabolized to dopamine elsewhere, causing 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 in five years after 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 averaging three to four times a day. 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. Besides, the trial 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

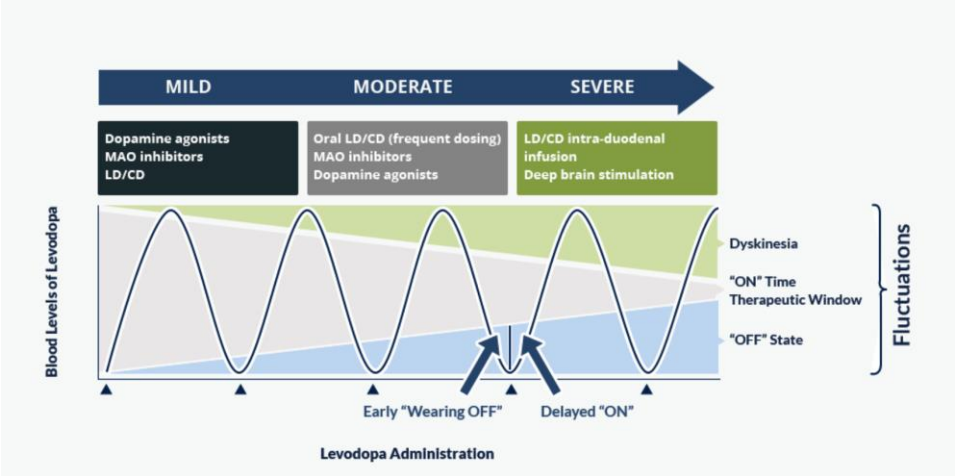


Comparison of Discontinuations



Source: PD MED Collaborative Group, 2014

Long-term Levodopa use is invariably associated with the development of dyskinesias that become as disabling as the PD symptoms themselves. Dyskinesias result 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. LID 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 LID after 3 years on L-DOPA 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 PD-LID was approved by the FDA in 2017 (Gocovri from Adamas Pharma), the most common treatment for LID is to reduce the dose of Levodopa. However, reducing the dose of Levodopa causes increased parkinsonism and worsening motor performance. Therefore, once established, LID becomes difficult to treat.

Pipeline: Focus on CNS related indications

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, mGluR5NAM proved to be a vailidated target following recent new insight on Novartis' mavoglurant 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.

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						Top line data Q3 2021
Dipraglurant-ER (mGlu5NAM)	Dystonia						
ADX71149 (mGlu2 PAM)	Epilepsy	janssen					
$GABA_B$ 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

In this report we will focus on the development of Dipraglurant in PD-LID and the upcoming pivotal trial. The development of its other programs are described in our previous report of 27 August 2019.

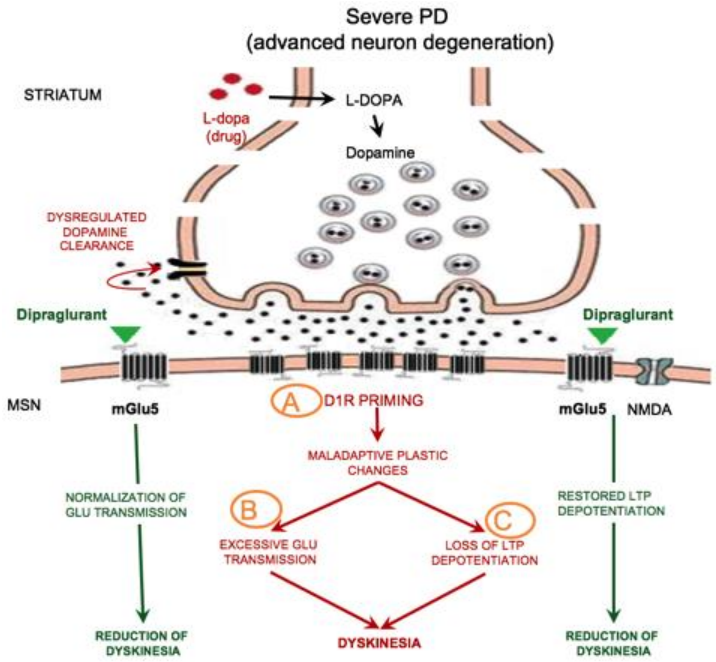
Dipraglurant IR in PD-LID

Addex lead program, dipraglurant for PD-LID has seen a dramatic increase in its market potential due to increased pricing, a clearer view on the number of patients, receipt of orphan drug designation from the FDA. The program is fully funded and 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 (mGluR5) 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.

Mechanism of Action of Dipraglurant

As mentioned earlier, the loss of substantia nigra neurons combined with the non-physiological pulsatile stimulation of dopamine receptors are at the basis of LID development.



In the striatum, LID is caused by:

- A: D1 receptor priming
- B: Abnormal glutamate transmission
- C: Loss of LTP depotentiation

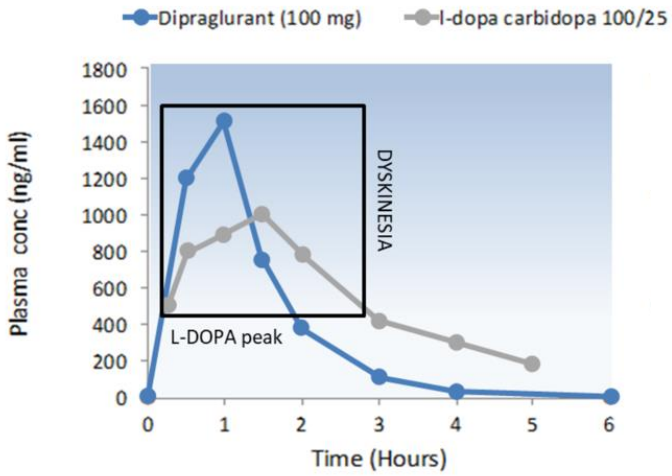
Metabotropic glutamate receptors, or mGluRs perform a variety of functions in the central and peripheral nervous systems: For example, they are involved in learning, memory, anxiety and the perception of pain. They are attractive drug targets due to their modulatory action to normalize glutamatergic activity and the restoration of LTP depotentiation. mGluR5 receptors are implicated in the control of glutamate transmission. Glutamate is a powerful excitatory neurotransmitter that is released by nerve cells in the brain. It is responsible for sending signals between nerve cells, and under normal conditions it plays an important role in learning and memory. Data, also from the Phase II study with Dipraglurant showed that mGluR5 blockade controls dyskinesia.

Unique Pharmacokinetic profile of Dipraglurant

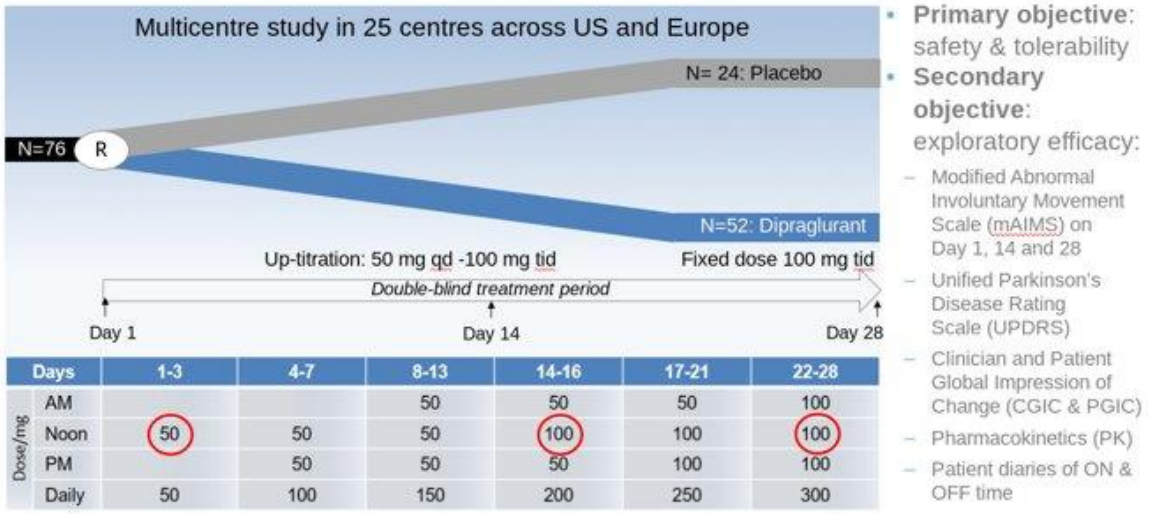
Addex has specifically developed an immediate release (IR) formulation of dipraglurant that mimics the uptake of levodopa in patients, since peak-dose dyskinesia is the most frequent levodopa-induced dyskinesia. Levodopa has to be given 3-4 times a day due to its relatively short half-life. Peak plasma 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



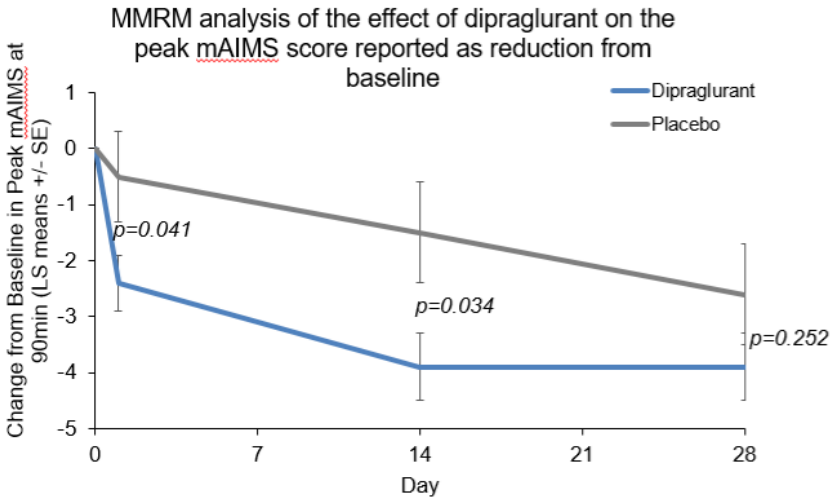
In a double-blind, placebo-controlled, US and European Phase II study in PD-LID, data showed that dipraglurant met the primary objective of the study by exhibiting a good safety and tolerability profile. Dipraglurant also demonstrated a statistically significant reduction in LID severity with both 50 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.



Days		1-3	4-7	8-13	14-16	17-21	22-28
Dose/mg	AM			50	50	50	100
	Noon	50	50	50	100	100	100
	PM		50	50	50	100	100
	Daily	50	100	150	200	250	300

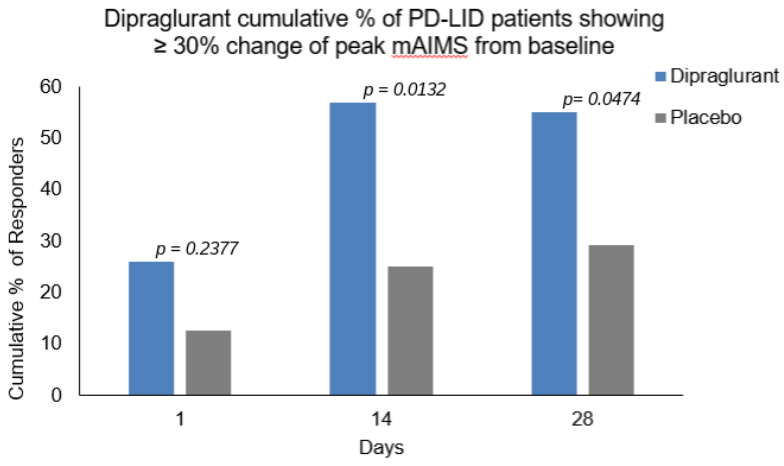
This study found that dipraglurant therapy resulted in substantial improvements on multiple efficacy endpoints. Patients taking dipraglurant had significant reductions in modified Abnormal Involuntary Movement Scale (mAIMS) during peak levodopa concentrations and this response was maintained during the 3-hour post-dosing

period. Participants receiving 50 mg dipraglurant on day 1 had a 19.9% reduction in mAIMS as compared to 4.1% for placebo (p = 0.042). After being titrated up to a 100 mg dose of dipraglurant, participants experienced a 32.3% reduction in mAIMS as compared to 12.6% for placebo (p = 0.034) on day 14. On day 28 the effect of the 100mg dose was maintained, however the study lost statistical significance due to an increased placebo response.



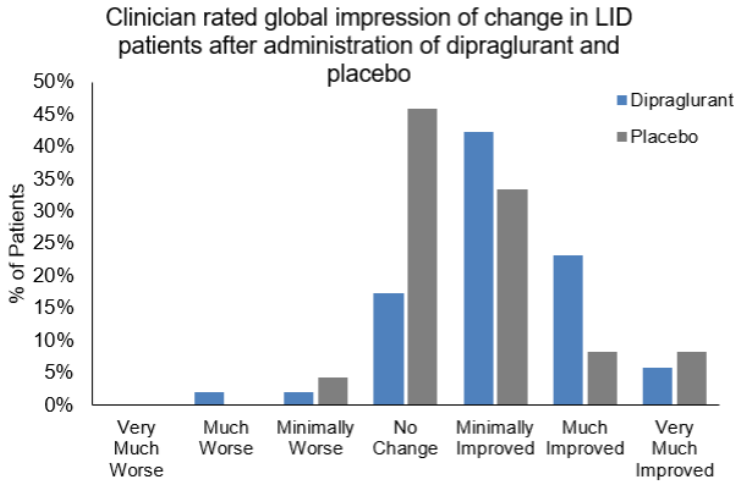
Source: Addex Therapeutics

Responder analysis measuring the cumulative percentage of patients showing a 30% change in peak mAIMS from baseline demonstrated dipraglurant 100mg dose had a significant benefit at both day 14 and day 28, which reinforces the robustness of dipraglurants anti-dyskinetic effect.



Source: Addex Therapeutics

When looking at Clinical Global Impression of Change (CGIC), there was even a greater improvement in dyskinesia with dipraglurant according to clinicians ($p < 0.05$). CGIC is a relatively simple scale that reflects the everyday clinical practice. The assessment is done by the treating physician which makes it a more objective assessment than the more subjective mAIMS.



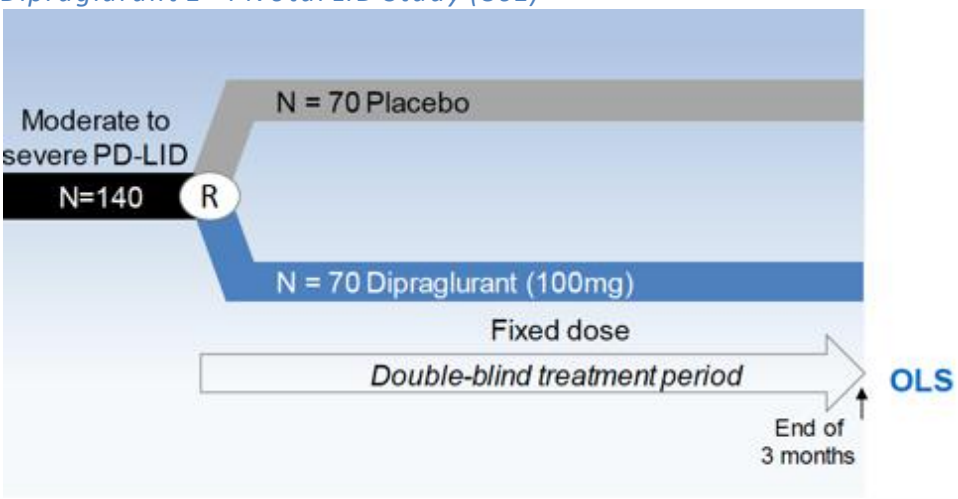
Source: Addex Therapeutics

Upcoming Phase IIb/III study Dipraglurant

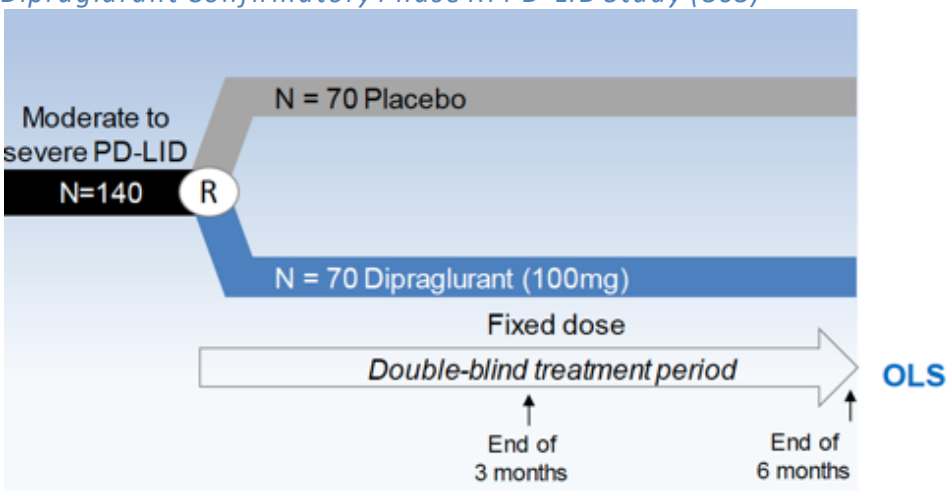
The company has launched a pivotal development program to support regulatory filing of dipraglurant in PD-LID with the first pivotal clinical trial starting in 2020Q1. This randomized, double blind, placebo-controlled Phase IIb/III pivotal registration study will assess the safety and efficacy of dipraglurant 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)



Financials

In 2019H1, Addex generated income of CHF 1.2 million research funding from Indivior for its research activities on GABAB PAM. The decrease of CHF 4.2 million compared to 2018H1 is due to the absence of the USD 5.0 million upfront payment received from its partner Indivior in January 2018. Research and development (R&D) expenses increased by CHF3.8 million to CHF5.9 million in the first-half 2019 compared to CHF2.1 million in the first-half 2018, primarily due to activities related to our dipraglurant Parkinson's and GABAB PAM programs. General and administrative (G&A) expenses increased from CHF0.8 million to CHF2.8 million in the first-half 2019, mainly due to share based compensation costs linked to equity incentive grants made at the end of the first-half 2018 and costs incurred in the first-half of 2019 related to preparing the anticipated listing of ADSs on the Nasdaq Stock Market. The net loss of CHF7.5 million in the first-half 2019, compared to a net income of CHF2.4 million for the first-half 2018, was due to a combination of increased R&D expenses and decreased income. Cash and cash equivalents at June 30, 2019 amounted to CHF36.7 million, compared to CHF43.6 million at June 30, 2018. The decrease is primarily due to the cash flows used in operating activities since July 1, 2018.

In October, Addex announced that Indivior PLC (LON: INDV) will provide Addex with an additional USD 800,000 in 2019 to accelerate research progress in their collaboration to develop further oral gamma-aminobutyric acid subtype B (GABAB) positive allosteric modulator (PAM) compounds for the treatment of addiction.

Profit & Loss Statement

CHF million	2017A	2018A	2018H1	2019H1
Revenues	0.500	6.701	5.368	1.227
R&D Costs	(2.629)	(4.920)	(2.084)	(5.894)
SG&A	(1.106)	(3.209)	(0.826)	(2.821)
Operating Profit/(Loss)	(3.235)	(1.425)	2.458	(7.488)
Finance result	(0.045)	(0.220)	(0.104)	(0.053)
Net Profit/(Loss)	(3.280)	(1.645)	2.354	(7.541)

Consolidated statement of cash flows

CHF million	2017A	2018A	2018H1	2019H1
Cashflow from operating activities	**(2.135)**	**1.752**	**3.583**	**(4.615)**
Cash flow from investing activities	**(0.02)**	**(0.062)**	**0.00**	**(0.024)**
Cash flow from financing activities	**3.355**	**37.390**	**37.458**	**(0.284)**
Cash and cash equivalents at beginning of the period	1.416	2.579	2.579	41.670
Net change in cash and cash equivalents	1.214	39.080	41.037	(4.924)
Cash and cash equivalents at the end of the year	2.579	41.670	43.563	36.748

Valuation and Share Price Performance

Stars are aligned for better performance in 2020

We are of the view that the current share price of Addex remains grossly undervalued. Since we initiated research coverage of Addex Therapeutics in October 2017, we frequently stated that the company is heavily underpriced. Unfortunately, in the last two years the share price did not show a positive performance, although fundamentally the company has become considerably stronger in terms of pipeline development, partnerships, management and cash position. In our view, the poor stock price performance in the last two years was due to a number of factors:

- Lack of news flow related to progress in the clinical pipeline – the company has been busy preparing the start of the dipraglurant PD-LID phase IIb/III program including manufacturing
- Limited equity research coverage and investor relations activities – following the CHF40 million financing in March 2018, management has been focused on executing on their strategy
- A wait-and-see approach regarding its late stage program dipraglurant in PD-LID – investors are waiting to see the Phase IIb/III start dosing patients
- The structure of the financing and retail investor base. We believe the inclusion of a seven year warrant in the March 2018 financing encouraged some investors to sell the underlying shares. This created weakness in the stock in 2018 which in turn stimulated selling by the retail investor base.
- In February 2019, the set-back with the Indivior partnership, when ADX71441 was terminated, increased uncertainty with investors in Addex. However, in reality this only resulted in a delay since Indivior are funding a research program at Addex to discover novel GABAB PAM compounds, and in October 2019 announced an additional $800K of funding in addition to the $4 million of already committed funding.

Now at the end of 2019 we believe that the stars are aligned for a much better performance in 2020. First of all, with the initiation of its pivotal clinical trial with dipraglurant in PD-LID in 2020Q1, the risk of the study not starting will have been removed and the focus will be much more on the substantial value a positive clinical trial outcome could create. Secondly, the company has filed for a dual listing on the NASDAQ which should have a positive effect on the visibility towards US investors. Thirdly, its visibility with Swiss investors will also likely increase as one Swiss bank already started coverage on Addex and we could reasonably expect more banks to follow. Fourthly, with an ongoing pivotal clinical trial ongoing the company management are likely to increase their investor relations activities which is likely to have a positive impact. Finally, with enough cash to fund its pivotal clinical trial of dipraglurant in PD-LID, its ongoing partnership with Indivior in addiction, and its

recent Eurostars grant award to fund its mGlu7NAM program in PTSD, the company has set up several programs which are likely to generate news worthy acheievements.

Valuation slightly increased with start of pivotal clinical trial imminent

We value Addex Therapeutics at **CHF 395-430 million or CHF 12.00-13.10** per share based primarily on the risk adjusted NPV of Dipraglurant for 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. We estimate that a peak market share of 25-30% is possible and a higher LOA of 25% as we believe that the vast amount of data justifies this. This leads to a total valuation for dipraglurant of CHF 345 million or CHF 10.50 per share. In addition, we have included the partnership with Indivior by taking into account the future milestones (USD 330 million) 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 50-85 million or CHF 1.75-3.00 per share. We did NOT include a value for the Dystonia Program as Addex is currently completing preclinical evaluation of dipraglurant in this disease area.

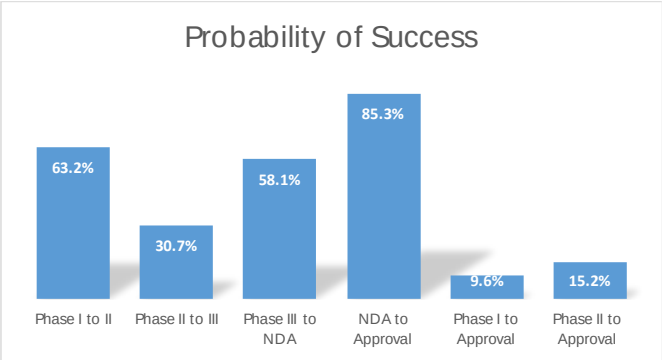
Another measurement for the potential value of Addex Therapeutics, is making a comparison with companies that have programs in development in PD-LID (dipraglurant), Parkinson's and Addiction since we believe these programs to be the most promising. We should note that in the past few years there has 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. Foliglurax is currently in Phase II for the treatment of PD.

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. Currently in Phase II.
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)

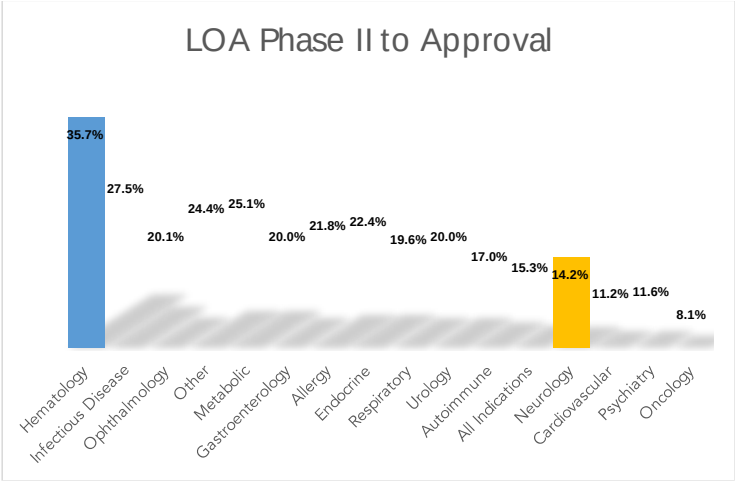
In estimating a value for the clinical programs with dipraglurant, we made use of several studies that were done on the clinical development success rates for investigational drugs to measure success rates for investigational drugs. We analyzed individual drug program phase transitions from January 1, 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.

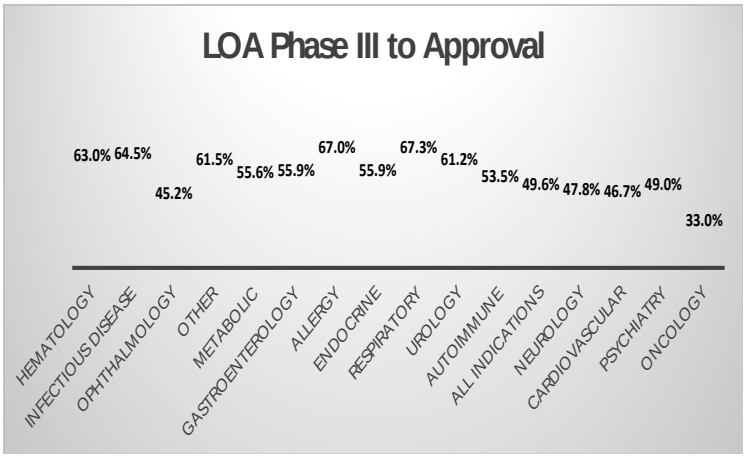
The Phase I transition success rate was 63.2% (n=3,582). As this Phase is typically conducted fo safety testing and is not dependent on efficacy results for candidates to advance, it is common for this phase to have the highest success rate among the clinical phases across most categories analyzed in 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.

Valuation in PD-LID US Market

Year	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	
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	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	
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**

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.