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VALUATIONLAB
FINANCIAL ANALYSIS

NEWRON PHARMACEUTICALS

FOCUS AREA: DISEASES OF THE CENTRAL NERVOUS SYSTEM (CNS) AND ORPHAN DISEASES

KEY DATA			SIX: NWRN
MARKET CAPITALIZATION (CHF MN)	38	**PRICE ON 5 MAY 2021**	2.2
ENTERPRISE VALUE (CHF MN)	4	**RISK-ADJUSTED NPV PER SHARE** (CHF)	10.7
CASH (31 DECEMBER 2020) (CHF MN)	35	**UPSIDE/DOWNSIDE** (%)	398%
MONTHLY OPERATING EXPENSE (CHF MN)	2.1	**RISK PROFILE**	HIGH RISK
CASH LIFE (YEAR)*	EARLY 2023	**SUCCESS PROBABILITY LEAD PIPELINE DRUG**	15%
BREAK-EVEN (YEAR)	2023	**EMPLOYEES** (GROUP)	24
FOUNDED (YEAR)	1998	**LISTED** (YEAR)	2006
KEY PRODUCTS:	**STATUS**	**MAJOR SHAREHOLDERS:**	**(%)**
- XADAGO (PARKINSON'S DISEASE; MAJOR INDICATION)	MARKETED	- ZAMBON GROUP	4.4
- XADAGO (PD-LID**; ORPHAN INDICATION)	PHASE III (Q1 2022)	- EXECUTIVE MANAGEMENT	0.6
- EVENAMIDE (SCHIZOPHRENIA; MAJOR INDICATION)	PHASE III (Q1 2022)	**- FREE FLOAT**	**99.4**
- EVENAMIDE (CTRS***; ORPHAN INDICATION)	PHASE III (Q1 2022)	- AVERAGE TRADING VOLUME (30-DAYS)	51,469
UPCOMING CATALYSTS:	**DATE**	**ANALYST(S):**	BOB POOLER
- EVENAMIDE - "STUDY 008A" (30 MG BID DOSE) RESULTS	END 2021		BP@VALUATIONLAB.COM
- EVENAMIDE - START PIVOTAL TRIALS SCHIZOPHRENIA/CTRS***	Q1 2022		+41 79 652 67 68
- XADAGO - START NEW LABEL TRIAL IN PD-LID**	Q1 2022		

* EUR 40 MN EUROPEAN INVESTMENT BANK LOAN EXTENDS CASH AND CASH LIFE CONSIDERABLY; ** PD-LID = PARKINSON'S DISEASE LEVODOPA-INDUCED DYSKINESIA; *** CTRS = CLOZAPINE TREATMENT-RESISTANT SCHIZOPHRENIA

ESTIMATES AS OF 5 MAY 2021

SOURCE: VALUATIONLAB ESTIMATES, NEWRON PHARMACEUTICALS

Down, but not out!

Schizophrenia and PD-LID trials start Q1 2022

Newron Pharmaceuticals has a product pipeline that targets diseases of the peripheral & central nervous system (CNS) and rare diseases. Key value drivers include: 1) Xadago, a once daily oral add-on therapy for Parkinson's disease with a unique dual mechanism of action, launched in the EU (2015), US (2017) and Japan (2019), with a potential new label extension in PD-LID (Parkinson's disease levodopa-induced dyskinesia), an orphan-like indication; and 2) evenamide, an add-on therapy for schizophrenia and CTRS (clozapine treatment-resistant schizophrenia, an orphan-like indication). Following the setback of sarizotan in Rett syndrome in May 2020, Newron will prioritize the evenamide late-stage development program in schizophrenia and CTRS. With cash and current financial assets of EUR 31.3 mn (31 December 2020), EUR 15 mn undrawn from the EUR 40 mn EIB (European Investment Bank) loan, and increasing Xadago revenues, Newron sees a cash runway to early 2023. The company is adequately funded beyond key value inflection points, including two potentially pivotal phase III trials with evenamide in schizophrenia and CTRS, and the Xadago line extension trial in PD-LID. We derive a sum-of-parts risk-adjusted (r)NPV value of CHF 10.7 per share with 39% of the value related to Xadago, 47% to evenamide, and 14% to cash. Newron's risk profile is High Risk as the company is loss making and revenues stem solely from Xadago royalties in Parkinson's disease.

Key catalysts:

- **Results evenamide FDA explanatory safety "Study 008A" (end 2021):** with 30 mg BID therapeutic evenamide dose - required by the FDA to address concerns of CNS events seen in animals before starting pivotal trials in schizophrenia and CTRS.
- **Start potentially pivotal program of evenamide in schizophrenia/CTRS (Q1 2022):** Our rNPV for evenamide in schizophrenia/CTRS jumps by CHF 16.4/share with a 50% (potentially pivotal) success rate from currently CHF 7.0/share with a 15% (POC) success rate.
- **Start new label trial Xadago in PD-LID (Q1 2022):** Our rNPV for Xadago in PD-LID rises by CHF 1.3/share with a 65% (phase III) success rate from currently CHF 0.4/share with a 15% (proof-of-concept - POC) success rate.

Recent Developments

Since our last Newron Valuation Report in September 2020, the company has nearly completed the FDA's request for additional safety data for evenamide before starting the phase III program. To fully comply with the FDA request, a final safety and efficacy "Study 008A" using the 30 mg BID (twice daily) evenamide therapeutic dose in schizophrenia patients will start in May with results expected by end 2021. The phase III program for evenamide in schizophrenia is slated to start in Q1 2021. Newron continues to evaluate potential options for partnering/co-developing the further development of evenamide.

An agreement was signed with partner Zambon for a phase III trial of Xadago in PD-LID, an important label extension and major differentiation for Xadago in key markets, with the trial now expected to start in Q1 2022. A Paragraph IV ANDA was filed by a generic manufactured for Xadago in the US to acquire "first-to-file" rights, underlining the differentiated nature of Xadago and its US peak sales potential, in particular, if the label is extended to treat patients with PD-LID.

The start of the phase III programs for evenamide in schizophrenia and Xadago in PD-LID will trigger significant upside to our rNPV based on substantially higher success rates of 50% and 65%, respectively, from currently 15%.

FY 2020 results came broadly in line with Newron extending its cash life to early 2023 from previously well into 2022.

May 4 – Newron reports the filing of a Paragraph IV ANDA for Xadago in the US
Newron reported a Paragraph IV Notice Letter was filed by a generic manufacturer of an Abbreviated New Drug Application to the FDA seeking approval to engage in the commercial manufacture, use or sale of safinamide mesylate drug product (branded "Xadago" by Newron) in the US before expiration of Xadago's US patents. Xadago is protected by three separate patents listed in the FDA Orange Book, including patent number "8283380" (expiry September 2027), "8278485" (expiry July 2027) and "8076515" (expiry November 2028), all with a patent use code U-1993 (adjunctive treatment to levodopa/carbidopa in patients with Parkinson's disease experiencing "off" episodes). Newron has 45 days to respond with an infringement suit against the generic manufacturer, which automatically postpones FDA approval of the generic by 30 months. We believe the listed patents in the FDA Orange Book provide strong protection until at least November 2028, with further protection through patent term extensions and potentially 7 years orphan drug market exclusivity upon US approval of Xadago in PD-LID. We maintain our US Xadago forecasts with patent expiry in 2031.

In our view, the Paragraph IV ANDA filing by the generic manufacturer is to acquire the so-called "first-to-file" right, the exclusive right to market the generic drug for 180 days before other generic versions may enter the US market. This is typically important for large-selling branded drugs. Therefore, we believe the Paragraph IV ANDA filing underlines the differentiated nature of Xadago due to its glutamatergic effect and the potential label extension for treating PD-LID, which would be a major differentiation for Xadago in key markets boosting global peak sales to more than EUR 400 mn in all indications.

April 23 – AGM - Shareholders approve FY 2020 balance sheet
Shareholders approved Newron's Balance Sheet as of 31 December, including related and consequent resolutions, the sole motion on the agenda of the 2021 Annual General Meeting.

April 1 – FDA required studies show evenamide met all safety objectives
Initial results from two short-term explanatory studies in evenamide: "Study 010" in healthy volunteers and "Study 008" in patients with schizophrenia, required by the FDA before starting the phase III program in schizophrenia, met the primary objective of safety and efficacy on all safety variables. Data from "Study 008" is a key component in the data package submitted to the FDA to support approval to start Newron's pivotal phase III trial program for evenamide in schizophrenia. Preclinical results confirming absence of toxicity were already submitted to the FDA to support this data package.

> **"Study 010":** A four-week, single dose, cross-over Thorough QT (TQT) study in 56 healthy volunteers, was designed to evaluate the effects of evenamide 30 mg and 60 mg (twice the therapeutic dose), compared to placebo and the antibiotic moxifloxacin 400 mg on the QT segment specifically, and on the electrocardiogram (ECG) generally, as requested by the FDA and under the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH). The results indicate that evenamide was devoid of any QTcF prolongation compared to placebo (indicating lack of any increased risk of arrythmia), while moxifloxacin was associated with a 17.3 ms median maximum increase suggestive of clinically significant risk of arrhythmia. These results strongly suggest that evenamide does not increase a patient's risk of QTc prolongation and arrhythmias, a risk generally associated with antipsychotics.
>
> **"Study 008":** A four-week, randomized, double-blind placebo-controlled study was designed to primarily evaluate the safety, tolerability, and electroencephalogram (EEG) effects of two fixed doses of evenamide, 7.5 mg and 15 mg BID (twice daily). The study was requested by the FDA to address questions which arose from a study of evenamide in rats, and central nervous system (CNS) events observed following high-dose administration of evenamide in dogs. "Study 008" was performed in 138 outpatients with chronic schizophrenia, receiving treatment with a second-generation atypical antipsychotic at study centers in the US and India. Over 95% of the patients completed the study. No patient on evenamide discontinued from the study due to adverse events, and there were no significant adverse events relating to evenamide. No symptoms were observed suggestive of severe CNS events, symptoms/signs of seizures, EEG diagnosis of seizure-like activity, or cardiac events in patients with evenamide. There were no differences in laboratory, ECG or vital signs abnormalities between evenamide and placebo-treated patients. The most frequent adverse events observed were related to CNS, gastrointestinal disorders, psychiatric disorders, metabolism and nutrition disorders and laboratory investigations. The most frequent adverse events reported (greater than 5%) were headache and somnolence, which were equally distributed between evenamide and placebo.

"Study 008" was designed to primarily assess safety and was not powered to demonstrate efficacy. The 7.5 mg BID was a "no-effect" dose, which will not be investigated further as expected. The 15 mg BID dose showed a higher response on the total PANSS than 7.5 mg BID, however, this was not statistically significant when compared to placebo.

The safety of the 30 mg BID therapeutic dose of evenamide will be assessed in an additional safety and efficacy "Study 008A" in patients with schizophrenia, to fully comply with the FDA's original request prior to starting the phase III program. "Study 008A" will start in May with results expected by end 2021. Following positive "Study 008A" results, the phase III program for evenamide in schizophrenia is expected to start in Q1 2022.

March 16 – FY 2020 results in line with cash life extended to early 2023
Newron reported a net loss of EUR 21.0 mn in 2020 compared to a net loss of 20.2 mn in 2019. Xadago royalty income increased by 10% to EUR 5.2 mn. Revenues were down 25% due to the absence of substantial license income in 2020. R&D expenses were down 15% largely due to the termination of the development program of sarizotan in Rett syndrome. Due to substantial changes of the regulations covering the Italian R&D tax credits, only EUR 1.4 mn could be accrued in 2020 compared to EUR 5.0 mn in 2019. The cumulated EUR 15.9 mn Italian tax credits can be offset with future tax and social contribution payments by Newron. In 2020, Newron received a third tranche of EUR 7.5 mn from its EUR 40 mn financing agreement with the EIB (European Investment Bank) with two tranches of EUR 15 mn remaining. Cash and cash equivalents at year-end 2020 amounted to EUR 31.3 mn.

FY 2020 results in a nutshell:

(in EUR mn)	**FY 2020**	**FY 2019**
License income	0	2.3
Royalties	5.2	4.7
Revenues	**5.3**	**7.0**
R&D expenses	-14.9	-17.4
Operating loss	-18.1	-20.9
Financial result	-1.6	0.7
Net loss	**-21.0**	**-20.2**
Cash and cash equivalents (year-end)	**31.3**	**39.2**

Outlook for 2021: Cash and cash equivalents, including the EUR 15 mn EIB funds not yet drawn down, in addition to its royalty income from Xadago and Italian tax credits, are sufficient to fund Newron's planned clinical development programs for evenamide and Xadago and operations to early 2023.

Evenamide: all preclinical studies requested by the FDA have been completed with no toxicity concerns. Enrolment was completed for explanatory "Study 008" with evenamide in schizophrenia patients with positive results reported in April 2021 (see above). An additional safety and efficacy "Study 008A" with the 30 mg BID (twice daily) evenamide therapeutic dose will start in May with results expected by end 2021 to fully comply with the FDA safety requests before starting the phase III program. We expect Newron to sign a lucrative (co)development and commercialization agreement with a major CNS player following positive "Study 008A" trial results. The pivotal phase III program in schizophrenia is on track to start in Q1 2022.

Xadago (safinamide): Supernus Pharmaceuticals acquired the CNS portfolio of US Worldmeds, including US rights of Xadago in June 2020. In March 2021, an agreement was signed with partner Zambon for the potentially pivotal global trial of Xadago in PD-LID, which is expected to start in Q1 2022.

Sarizotan in Rett syndrome: was terminated after the pivotal "STARS" program did not meet its primary endpoint in May 2020.

March 15 – Agreement signed with Zambon for potentially pivotal Xadago PD-LID trial
An agreement was signed with partner Zambon to start a potentially pivotal trial to evaluate the efficacy of safinamide (branded "Xadago" in the US) in Parkinson disease patients with levodopa-induced dyskinesia (PD-LID). The double-blind, placebo-controlled trial will be conducted in the US, Europe and Asia/Australia, with the aim of an important label extension and differentiation for safinamide in key markets. Newron and Zambon will share the costs of the trial equally, and in return, Newron will qualify for a one-time milestone payment and a greater share of royalties should the trial lead to a label extension. As PD-LID is considered an orphan indication in the US, this also allows for faster review times. The PD-LID trial is expected to start in Q1 2022 with topline results expected two years later. We forecast peak sales of Xadago in PD-LID to amount to around EUR 200 mn, with first launches to occur in 2024.

Strategy & Cash Position

Italian biopharmaceutical company specialized in CNS and rare diseases
Newron Pharmaceuticals S.p.A. is an Italian biopharmaceutical company specialized in prescription drugs to treat peripheral & central nervous system (CNS) disorders and rare, so-called orphan diseases, with an expertise in ion channel blockers, an important class of CNS drugs. Newron is based in Bresso, near Milan, Italy and was established in December 1998 as a spin-off from Pharmacia & Upjohn (now part of Pfizer). In 2014, the company opened a US office in Morristown, New Jersey, USA. Currently, the group has 24 employees. Newron was listed on the SIX Swiss Stock Index in 2006 with the ticker code: NWRN. In addition to the primary listing in Switzerland, Newron began trading in Germany on the Düsseldorf Stock Exchange and XETRA (ticker code: NP5) to facilitate access for investors based in the EU via EU brokers in 2019.

Strategy to develop CNS drug to optimal value, then out-license major indications and preferably market orphan indications by an own small specialist sales force
Newron's strategy is to develop drugs originated from earlier discovery capabilities, acquire or in license CNS disease drugs and develop them to their optimal value, and in case of rare diseases like evenamide in clozapine treatment-resistant schizophrenia (CTRS), whenever possible commercialize them to optimize long-term value. Where necessary or advantageous, the company seeks co-development and commercialization agreements to reduce research and development costs and generate revenue through R&D funding, milestone payments and royalties on future sales.

Newron's pipeline consists of a nice mix of major and rare disease indications
Newron has an attractive pipeline with multiple catalysts on the horizon despite the recent setback with sarizotan in Rett syndrome in May 2020 where the pivotal "STARS" trial did not reach its endpoints. Newron's pipeline consists of a nice mix of major indications, such as Xadago that already generates revenues though its partners in Parkinson's disease and evenamide as an add-on to antipsychotics in schizophrenia, and orphan-like indications, such as Xadago in PD-LID (Parkinson's disease levodopa-induced dyskinesia) and evenamide in CTRS (clozapine treatment-resistant schizophrenia). Currently, the majority of Newron's valuation is based on the (low) sales royalties and milestone payments from its partners for Xadago in Parkinson's disease. Substantial value will be unlocked with the approval and launch of evenamide in schizophrenia with blockbuster sales potential. Newron's individual product strategy includes:

- **Evenamide – New paradigm in schizophrenia, transformational potential**
  Evenamide is Newron's pipeline project with the highest peak sales potential targeting a USD 12 bn schizophrenia market and will be transformational for Newron upon approval. In 2017, evenamide established proof-of-concept (POC) as an add-on to current antipsychotics in patients with schizophrenia. Discussions with key opinion leaders and regulators highlighted the potential of evenamide as a new treatment paradigm for schizophrenia. A fast-to-market development pathway was recognized by parallel development of evenamide in schizophrenia, a major indication with limited effective and well tolerated treatment options, as well as in clozapine treatment-resistant schizophrenia (CTRS), an orphan-like indication with high unmet medical need with the potential for accelerated approval. Based on these findings Newron raised CHF 27 mn

in September 2017 to fund these new development plans instead of out licensing evenamide to a major CNS player on POC results on lower terms. Consequently, evenamide could be on the market at far better licensing terms with the potential to market evenamide in CTRS by an own specialist sales force in the US, optimizing the long-term potential substantially. In May 2019, Newron was on the verge of starting the two potentially pivotal efficacy trials, one in patients with schizophrenia experiencing worsening of psychosis on atypical antipsychotics ("Study 003") and another in CTRS ("Study 004"), when it received a communication from the FDA indicating concerns on potential safety issues seen in a study with rats and CNS events at high doses in a study with dogs. Newron was requested to delay the start of the two pivotal trials until these concerns were adequately addressed.

All evenamide pre-clinical trials requested by the FDA have now been completed with no toxicity concerns identified. In April 2021, Newron reported positive results of "Study 008" in 138 schizophrenia patients. Data from "Study 008" is a key component in the data package submitted to the FDA to support approval to start Newron's pivotal phase III trial program for evenamide in schizophrenia. No symptoms were observed suggestive of severe CNS events, symptoms/signs of seizures, EEG diagnosis of seizure-like activity, or cardiac events in patients with evenamide. There were no differences in laboratory, ECG or vital signs abnormalities between evenamide and placebo-treated patients. The CNS events appear to be a known "class effect" with sodium channel blockers in animal studies, which also occurred with Xadago and were ultimately resolved. In May, the company will start an additional safety and efficacy clinical trial required by the FDA, called "Study 008A" with the 30 mg BID therapeutic dose of evenamide with results expected by end 2021. Newron is confident it can start pivotal development of evenamide in schizophrenia and CTRS in Q1 2022. The company is currently evaluating options for partnering or co-developing evenamide upon confirmation of prior proof-of-concept by "Study 008A" as early as end 2021 or early 2022.

- **Xadago – Global rollout and PD-LID label extension to boost sales uptake**

  Xadago (safinamide) is Newron's first-ever approved drug for treating patients with mid to late stage Parkinson's disease and was launched by its partners in the EU in 2015 and in the US in 2017, and in Canada (branded Onstryv) and Japan (branded Equfina) in 2019. Xadago stems from Newron's earlier ion channel discovery capabilities and is the first New Chemical Entity (NCE) approved and launched for treating Parkinson's disease in over a decade. The company receives sales royalties and milestone payments from its development and commercialization partners Zambon (worldwide rights excluding Meiji Seika territories) and Meiji Seika (Japan and Asia). Uptake in the lucrative US market (now marketed by Supernus Pharma) is hampered by widespread cheap generic versions of Teva's Azilect (rasagiline), which belongs to the same drug class as Xadago.

  With an agreement signed in March 2021, Newron and Zambon plan to expand Xadago's label to include PD-LID, a lucrative orphan-like indication in the US with limited treatment options, thereby strengthening its label and boosting future sales uptake. Newron and Zambon will share the costs of the trial equally, and in return, Newron will qualify for a one-time milestone payment and a greater share of royalties on the overall Zambon sales should the trial lead to a label extension. The single, potentially pivotal PD-LID trial is expected to start in Q1 2022 (delayed by Covid-19 pandemic) with results expected two years later.

Down, but not out – sarizotan setback in Rett syndrome narrows Newron's CNS focus
In May 2020, Newron suffered a major setback with sarizotan in treating breathing disturbances in girls with Rett syndrome, a rare but severe genetic neuro-development disorder affecting females with approximately 15,000 patients in the US and 20,000 in the EU. Sarizotan had the potential be the first-ever treatment approved for Rett syndrome with the promise of a life-modifying drug for these patients based on exciting data from Rett syndrome animal models. Unfortunately, the promising animal data did not translate into humans. The single pivotal phase III "STARS" trial did not meet its primary and secondary endpoints in reducing breathing difficulties in these patients. Sarizotan was discontinued leading to a sharp share price drop with Newron currently trading below Enterprise Value. Although the odds were against this promising late stage project (we assumed a low 25% success rate), we believe development of sarizotan in Rett syndrome was justified by a relatively small investment (an estimated EUR 30 mn in development costs), which could have amounted to substantial value creation. Sarizotan would have transformed Newron into a high margin CNS specialty biopharmaceutical company likely reaching profitability as early as 2021. We forecasted peak sales of EUR 400+ mn, with the company building up an own small specialist in key markets to maximize profitability. Moreover, upon US approval of sarizotan in Rett syndrome, Newron would have been eligible for a Rare Disease Pediatric Priority Review (RDPPR) Voucher that could be sold freely for an estimated USD 100+ mn, which could easily have funded the buildup of the specialist sales force in the US and EU.

Evenamide targets blockbuster sales in schizophrenia with a higher success rate
Newron's priority now lies in the successful development of evenamide in schizophrenia/CTRS that targets a EUR 1.2+ bn peak sales market opportunity, which will also be transformational for the company. The company intends to establish an own small specialist sales force to market evenamide in the CTRS orphan indication in the lucrative US market. We assume Newron will out license the evenamide schizophrenia rights after completion of the two pivotal trials in return for substantial upfront, development and commercialization milestones and royalties on sales and commercialize evenamide in CTRS in the US through an own specialist sales force. Importantly, the historical success rate of evenamide in schizophrenia is 50% once the pivotal trials start in Q1 2022, double of the success rate for sarizotan in Rett syndrome. Note that the pivotal trials for evenamide are based on the compelling phase IIa POC results seen in 89 patients with schizophrenia, while the sarizotan pivotal trial was largely based on exciting data in a Rett syndrome animal model. The two pivotal trials are expected to cost approximately EUR 30 mn.

Newron's key priorities in the next 12-18 months, include:
- The continued rollout of Xadago in Parkinson's disease by its partners in new countries/areas and the signing on of new commercialization/distribution partners for Xadago beyond the EU, US, and Japan
- File an infringement suit against the generic manufacturer that filed a Paragraph IV ANDA for Xadago in the US
- Complete the short-term explanatory safety and efficacy "Study 008A" by end 2021 to fulfill the FDA safety requirements to start pivotal development of evenamide in schizophrenia and CTRS.
- Determine potential options for partnering or co-development of evenamide.
- Start the two single potentially pivotal phase IIb/III trials of evenamide: 1) "Study 003" an add-on to current antipsychotic therapy in schizophrenia (major indication), and 2) "Study 004" as an add-on to clozapine in patients with CTRS (orphan indication), in Q1 2022.

- Expand and strengthen Xadago's label to include PD-LID, a lucrative orphan-like indication, together with partner Zambon with the initiation of a single potentially pivotal efficacy trial in Q1 2022 (delayed by the COVID-19 pandemic).
- Seek new CNS development projects to replenish the company's development pipeline after the setback of sarizotan in Rett syndrome.
- Maintain timelines as much as possible despite the ongoing Covid-19 pandemic.

Almost EUR 270 mn raised since inception in 1998

Since inception Newron has been quite successful in raising money and has invested significant resources and time mostly in developing Xadago in Parkinson's disease and ralfinamide in neuropathic low back pain, and now sarizotan in Rett syndrome and evenamide in schizophrenia. The company raised EUR 267 mn, of which EUR 114 mn in several private placements, the latest in September 2017, raising CHF 27 mn with existing and new investors.

MONEY RAISED	EUR MN
PRE-IPO	62
IPO	74
GRANTS	14
PRIVATE PLACEMENTS	114
NEURONOVA ACQUISITION	16
TOTAL RAISED	**267**

SOURCE: VALUATIONLAB, NEWRON PHARMACEUTICALS

Prior to the IPO in 2006, management raised EUR 62 mn in three financing rounds. Newron was seed funded in 1999 by 3i with the company raising EUR 7 mn, followed with a EUR 25 mn B round (3i, Atlas, Apax) and a EUR 30 mn C round (3i, Atlas, Apax, HBM, TVM). Newron had one of the largest biotech IPO's in 2006 that provided the company with sufficient funds to develop ralfinamide up to phase IIb dose ranging trials in neuropathic low back pain. The NeuroNova acquisition added another EUR 16 mn to the cash position and committed cash-inflows in 2012.

European Investment Bank "Junker Plan" loan of up to EUR 40 mn

In October 2018, a financing agreement was signed with the EIB (European Investment Bank) that allows Newron to borrow up to EUR 40 mn over a period of several years subject to achieving a set of agreed performance criteria. The EIB loan is backed by the EFSI (European Fund for Strategic Investments), the central pillar of the Investment Plan for Europe, also known as the "Juncker Plan". The EIB loan underlines Newron's CNS pipeline potential and provides the company with additional financial flexibility to successfully execute its development and commercialization plans. The funds are intended to support the pivotal and post-approval stage CNS development programs. In June 2019, Newron received the 1st tranche of EUR 10 mn followed by a second tranche of EUR 7.5 mn in November 2019 and a third tranche of EUR 7.5 mn in April 2020. In connection with the three tranches received, the EIB has received warrants entitling it to purchase up to 504,481 ordinary shares of Newron at an exercise price of EUR 9.25 per share. The last two tranches of EUR 7.5 mn each have not been drawn down yet, providing additional financial flexibility.

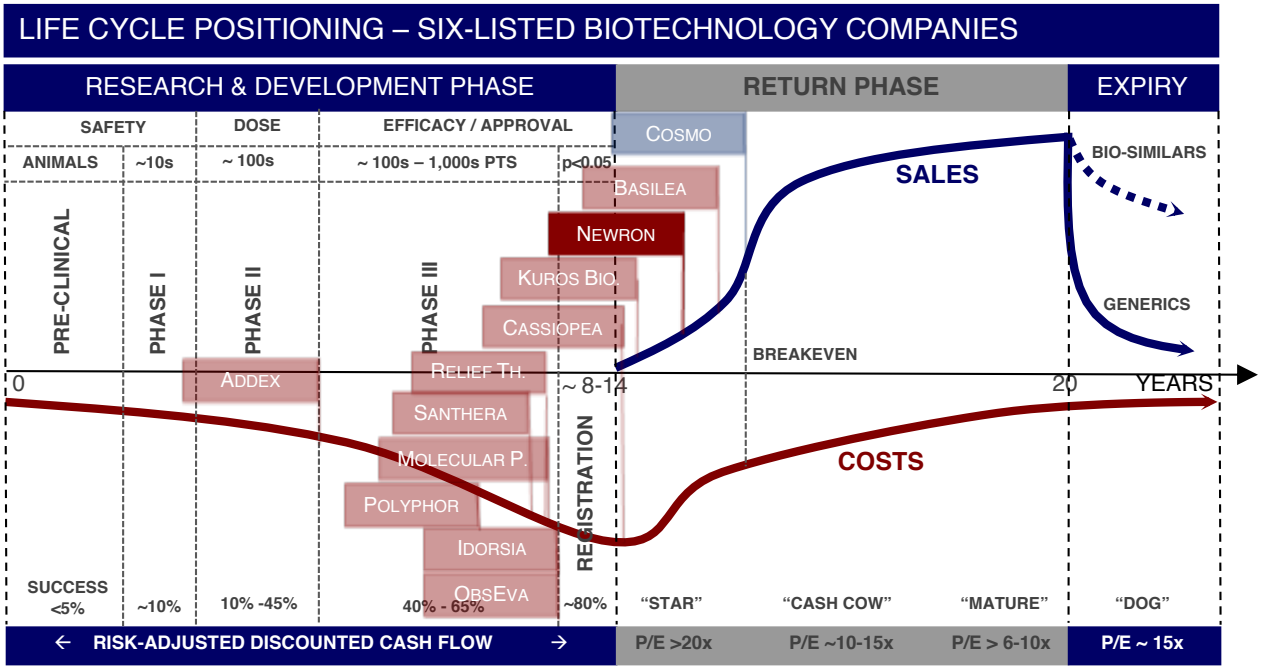
Newron sufficiently funded to approach profitability in 2023

We believe Newron is sufficiently funded to execute its current development plans and to approach profitability in 2023. With EUR 31.3 mn in cash and short-term investments (31 December 2020) together with the remaining two EIB loan tranches worth EUR 15 mn and

increasing royalty payments on Xadago sales, we calculate Newron should have sufficient funds to complete the two potentially pivotal trials of evenamide in schizophrenia and CTRS, with a total cost of approximately EUR 30 mn, as well as co-finance together with Zambon the potentially pivotal single trial for Xadago in PD-LID. Newron is currently evaluating potential options for partnering or co-developing evenamide in schizophrenia to potentially share the development risk, reduce the cash burn and replenish its cash position to increase financial flexibility, which can be used to broaden the pipeline with promising external CNS compounds.

Life Cycle Positioning – High Risk

We qualify Newron's risk profile as High Risk as the company is still loss making and revenues are solely dependent on Xadago. On reaching profitability in 2023 and successful completion of the pivotal development of evenamide in schizophrenia and CTRS, the company should see a re-rating of the risk profile to Medium Risk. (see Important Disclosures for our Risk Qualification).



SOURCE: VALUATIONLAB

Valuation Overview

Risk-adjusted sum-of-parts NPV points to a fair value of CHF 10.7 per share

We derive a sum-of-parts risk-adjusted NPV of CHF 10.7 per share, with cash of CHF 2.0 per share (31 December 2020), overhead of CHF 4.2 per share, using a WACC of 7% (reflecting the low Swiss interest environment).

SUM OF PARTS

PRODUCT NAME	INDICATION	PEAK SALES (EUR MN)	LAUNCH YEAR	UNADJUSTED NPV/SHARE	SUCCESS PROBABILITY	RISK-ADJUSTED NPV/SHARE (CHF)	PERCENTAGE OF TOTAL
XADAGO (SAFINAMIDE)	PARKINSON'S DISEASE	227	2015(EU) / 2017(US)	5.4	100%	5.4	37%
XADAGO (SAFINAMIDE)	PARKINSON'S DISEASE LEVODOPA-INDUCED DYKINESIA (PD-LID)	206	2024	2.6	15%	0.4	3%
EVENAMIDE	SCHIZOPHRENIA	1,067	2025	38.2	15%	5.7	39%
EVENAMIDE	CLOZAPINE TREATMENT-RESISTANT SCHIZOPHRENIA (CTRS)	132	2024	8.5	15%	1.3	9%
RALFINAMIDE	NEUROPATHIC PAIN	NON CORE		0			
CASH & CASH EQUIVALENTS (31 DECEMBER 2020)		31		2.0		2.0	14%
TOTAL ASSETS				**57.2**		**14.9**	**100%**
OVERHEAD EXPENSES				-4.2		-4.2	
NPV/SHARE (CHF)				**53.0**		**10.7**	
SHARE PRICE ON MAY 05, 2021						2.2	
PERCENTAGE UPSIDE / (DOWNSIDE)						398%	
ESTIMATES AS OF 5 MAY 2021						SOURCE: VALUATIONLAB ESTIMATES	

Newron's key value drivers, include:

Xadago (Parkinson's disease) - risk-adjusted NPV of CHF 5.4 per share

Xadago is Newron's first-ever drug to be approved and launched and marks the first new chemical entity (NCE) for Parkinson's disease in over a decade. The drug was launched in the EU (2015), in the US (2017) and in Japan (2019) to treat mid-to-late stage Parkinson's disease. In the lucrative US market, sales uptake continues to be hampered by cheap generic versions of Teva's Azilect (rasagiline), which belongs to the same drug class as Xadago. We assume Newron will receive a remaining EUR 10 mn in milestone payments from its partners Zambon (and sub-licensors) and Meiji Seika (and partner Eisai), with royalties on sales ranging between 10-15% in EU/ROW, 7.5% in the US, and 2.5% in Japan. We calculate an NPV of CHF 6.0 per share with peak sales of EUR 227 mn for Xadago in Parkinson's disease.

Xadago (PD-LID) – risk-adjusted NPV of CHF 0.4 per share

Newron and Zambon have decided to develop an important line extension of Xadago in PD-LID, an orphan-like disease with limited treatment options, to further strengthen Xadago's profile. We assume first launches in 2024, and conservatively assume similar pricing as for Xadago in Parkinson's disease. Based on conservative peak penetration rates ranging between 4-6% we derive peak sales of EUR 206 mn. We calculate a rNPV of CHF 0.4 per share for Xadago in PD-LID with a conservative 15% (proof-of-concept) success probability based on the findings in the registrational "Study016/018" Parkinson's disease trial where Xadago reduced dyskinesia in these patients.

NOTE: Our success probability will increase to 65% (phase III) with our rNPV jumping by CHF 1.3 per share on the start of the line extension trial of Xadago in PD-LID in Q1 2022.

Evenamide (schizophrenia) – risk-adjusted NPV of CHF 5.7 per share

Evenamide, a proprietary discovery project for treating schizophrenia, targets a global USD 12 bn antipsychotic market opportunity. Newron plans to develop evenamide as an add-on to antipsychotics in schizophrenia (major indication) and in CTRS (orphan-like indication). The company is confident it can start pivotal development in Q1 2022. The additional short-term safety and efficacy "Study 008A" trial with the evenamide 30 mg BID therapeutic dose

in schizophrenia patients, required by the FDA, is expected to report results by end 2021. The two potentially pivotal trials, “Study 003” in schizophrenia and “Study 004” in CTRS are now planned to start in Q1 2022 (both with 18 months to completion). On successful development in schizophrenia, we assume Newron to license the compound to a major CNS player in return for substantial upfront and sales milestone payments and royalties on sales. We forecast peak sales for evenamide to amount to EUR 1.1+ bn in its major indication schizophrenia. We assume first launches in early 2025 with annual treatment costs ranging between EUR 3,650 (EU/ROW) and USD 5,475 per patient with peak penetration rates ranging between 15-20%. We calculate a rNPV of CHF 5.7 per share with a conservative 15% (proof-of-concept) success rate, with Newron receiving EUR 273 mn in global upfront, development and sales milestones and 20% net sales royalties.

Evenamide (CTRS) – risk-adjusted NPV of CHF 1.3 per share

Newron’s development plans for evenamide to include CTRS next to schizophrenia were triggered by the high unmet medical need for CTRS treatments, studies suggesting the involvement of the glutamate system in CTRS, and US orphan disease designation. CTRS provides a fast-to-market indication (we expect first launches in 2024 based on accelerated approval) with 7-years orphan disease market exclusivity upon US approval. We assume Newron to commercialize evenamide in CTRS in the US through an own small specialist sales force and seek partners outside the US in return for EUR 20 mn upfront, development and sales milestones and 25% net sales royalties. We forecast peak sales to amount to EUR 132 mn assuming the same annual treatment cost as for schizophrenia and peak penetrations ranging between ~40% (EU/ROW) and ~50% (US) to reflect the high unmet medical need and lack of alternatives. Our risk-adjusted NPV amounts to CHF 1.3 per share with a conservative 15% (proof-of-concept) success rate.

NOTE: Our success rate for evenamide in schizophrenia and CTRS will increase to 50% when the two phase III trials starts in Q1 2022. Consequently, our rNPV for evenamide in schizophrenia/CTRS will jump by CHF 16.4 per share from currently CHF 7.0 per share. We conservatively use a 50% success rate instead of the historical 65% phase III success rate to reflect the potentially pivotal trial design with two cross-supportive phase III trials, one in schizophrenia (“Study 003”) and one in CTRS (“Study 004”).

Additional upside to our forecasts could come from higher pricing (e.g. USD 10-15,000/year in the US) if the results of the phase III program point to a new treatment paradigm with evenamide increasing quality of life and significantly reducing the social burden. In particular CTRS patients consume the most resources of all schizophrenia patients and would justify higher pricing if evenamide is effective.

Sensitivities that can influence our valuation

Development risk: With Xadago approved in the major markets, Newron's major risk is the development risk of its key pipeline projects, in particular evenamide as an add-on therapy for treating schizophrenia and CTRS. We currently have a conservative 15% (historical phase IIa POC) success rate for evenamide. Once the two pivotal trials start in schizophrenia and CTRS in Q1 2022, our success rate will jump to 50%, the estimated success rate for a CNS compound in phase II/III cross-supportive pivotal trials. Successful completion of evenamide in schizophrenia will be transformational for Newron. The necessary funds to develop evenamide in schizophrenia and CTRS as well as Xadago in PD-LID have been secured. Xadago phase III development in PD-LID will start in Q1 2022 with a historical 65% phase III success rate. The COVID-19 pandemic can lead to delays.

Pricing and reimbursement: Following EMA and FDA approval, Xadago must be priced and reimbursed by local health care providers. In the EU pricing and reimbursement occurs on a country-by-country base, which can lead to different pricing and reimbursement, and market launch delays. Pricing and reimbursement have been established in the US.

Partnering: In 2012, Newron out-licensed Xadago rights to Meiji Seika for Japan and Asia, and to Zambon that gained worldwide rights (excluding Meiji Seika territories). Zambon does not have a strong presence in all markets and will need to secure strong commercialization partners in these regions. Consequently, there is limited visibility on the timing and terms on which these sub-licensers will be contracted. In June 2020, Supernus Pharmaceuticals acquired the commercial rights of Xadago from US WorldMeds for the critical US market. We assume Newron to seek a (co)development and commercialization partner for evenamide in schizophrenia after successfully completing "Study 008A" by end 2021 in return for substantial upfront, regulatory and sales milestones and royalties on sales to share the development risk, reduce the cash burn and increase financial flexibility. Timing and terms could differ from our forecasts.

Commercialization: Newron's revenues and earnings for Xadago are entirely dependent on its commercialization partners to successfully position and market Xadago against existing Parkinson's treatments such as Teva's Azilect (rasagiline) and generic versions of rasagiline. Newron needs a major CNS partner to successfully commercialize evenamide in schizophrenia. Revenues and earnings for evenamide in schizophrenia will be entirely dependents on its commercialization partner to successfully position and market evenamide against existing and new treatments. Newron plans to build up an own specialist field force for evenamide in CTRS in the US, which could require additional funding.

Patent and market exclusivity: Xadago's composition of matter patent expired in 2010. Patent protection and market exclusivity beyond this period relies heavily on the combination patent with levodopa that runs until 2024 (EU) and 2026 (US) with extensions up to 5 years. A synthesis patent provides additional protection until 2027. We conservatively assume patent protection for Xadago until 2029 (including extension). Evenamide's patent protection runs until 2028 with extensions up to another 5 years. NCE (new chemical entity) exclusivity amounts to 5 years in the US, orphan disease exclusivity adds 7 years upon US approval, while data protection provides 10 years exclusivity in the EU. In May 2021, Newron reported a generic manufacturer filed a Paragraph IV ANDA for Xadago in the US, which could lead to generics entering the US market earlier than expected.

Catalysts

CATALYST TIMELINES

TIME LINE	PRODUCT	INDICATION	MILESTONE	COMMENT	IMPACT ON RNPV/SHARE
2021					
21 JAN	EVENAMIDE	SCHIZOPHRENIA	COMPLETE ENROLLMENT EXPLANATORY TRIAL	FULL ENROLLMENT OF 138 PATINETS COMPLETED IN SHORT-TERM EXPLANATORY "STUDY 008"; RESULTS EXPECTED BY END Q1 2021	
15 MAR	XADAGO	PD-LID *	ZAMBON AGREEMENT	AGREEMENT SIGNED WITH ZAMBON TO DEVELOP XADAGO IN PD-LID; NEWRON RESPONSIBLE FOR PHASE III CLINICAL DEVELOPMENT AND REGULATORY; COSTS WILL BE SPLIT EVENLY; NO COST CAP; NEWRON ENTITLED TO REGULATORY MILESTONE AND HIGHER ROYALTIES ON SALES THAN CURRENTLY	
16 MAR			FY 2020 RESULTS	CASH & CURRENT FINANCIAL ASSETS: EUR 31.3 MN (EXCLUDES EUR 15 MN UNDRAWN EIB LOAN); FUNDED INTO EARLY 2023 AND KEY VALUE INFLECTION POINTS; 2020 TOTAL REVENUES: EUR 5.3 MN FROM XADAGO ROYALTIES (+10%) FROM EUR 57 MN ESTIMATED XADAGO GLOBAL SALES; PIVOTAL TRIALS EVENAMIDE IN SCHIZOPHRENIA TO START Q3 2021; XADAGO IN PD-LID IN H2 2021	
1 APR	EVENAMIDE	SCHIZOPHRENIA	EXPLANATORY "STUDY 008" RESULTS	PRIMARY OBJECTIVE OF EVENAMIDE MET ON ALL SAFETY VARIABLES FOR "STUDY 008" IN PATIENTS WITH SCHIZOPHRENIA AS WELL AS FOR "STUDY 101" IN HEALTHY VOLUNTEERS AS REQUIRED BY THE FDA; ADDITIONAL SAFETY AND EFFICACY "STUDY 008A" WITH 30 MG BID EVENAMIDE THERAPEUTIC DOSE TO START IN APRIL TO FULLY COMPLY WITH FDA'S REQUEST BEFORE STARTING PHASE III PROGRAM	
13 APR			AGM	ALL PROPOSALS ACCEPTED AT ANNUAL GENERAL MEETING (VIRTUAL DUE TO COVID-19 PANDEMIC)	
MAY			START "STUDY 008A"	START SAFETY AND EFFICACY "STUDY 008A" WITH EVENAMIDE 30 MG BID (DESIGNATED AS THERAPEUTIC DOSE) IN SCHIZOPHRENIA PATIENTS TO FULLY COMPLY WITH FDA REQUEST PRIOR TO STARTING PHASE III PROGRAM	
Q2	EVENAMIDE	SCHIZOPHRENIA	REGULATORY DISCUSSIONS	DISCUSSION WITH FDA ON PRECLINICAL AND EXPLANATORY "STUDY 008" RESULTS TO REMOVE FDA CONCERNS OF CNS EVENTS SEEN IN HIGH DOSES IN ANIMALS	
Q2-Q4			4TH & 5TH TRANCHE EIB FINANCING	REMAINING TWO TRANCHES OF EUR 7.5 MN OF EIB LOAN WORTH UP TO EUR 40 MN	
16 SEP			H1 2021 RESULTS	PUBLICATION OF HALF-YEAR REPORT 2021	
END			RESULTS "STUDY 008A"	RESULTS "STUDY 008A" EVENAMIDE 30 MG BID (DESIGNATED AS THERAPEUTIC DOSE) IN SCHIZOPHRENIA PATIENTS REQUIRED BY FDA BEFORE STARTING PHASE III PROGRAM	
END 2021/ EARL 2022	EVENAMIDE	SCHIZOPHRENIA	POTENTIAL OUT LICENSING AGREEMENT(S)	AFTER POSITIVE "STUDY 008A" RESULTS WE EXPECT A POTENTIAL (CO-) DEVELOPMENT AND COMMERCIALIZATION AGREEMENT(S) WITH MAJOR CNS PLAYER(S) FOR MAJOR SCHIZOPHRENIA INDICATION TO ENHANCE DEVELOPMENT AND COMMERCIALIZATION, REDUCE CASH BURN AND STRENGTHEN CASH POSITION	
2022					
Q1	XADAGO	PD-LID *	START NEW LABEL TRIAL	START OF NEW LABEL TRIAL IN PD-LID (PARKINSON'S DISEASE LEVODOPA INDUCED DISKINESIA) EVENLY FUNDED WITH PARTNER ZAMBON - TIMING DEPENDENT ON POTENTIAL COVID-19 DELAYS	+ CHF 1.3
Q1	EVENAMIDE	CTRS **	PHASE IIB/III	START OF POTENTIALLY PIVOTAL TRIAL IN CLOZAPINE TREATMENT-RESISTANT SCHIZOPHRENIA PATIENTS (ORPHAN INDICATION) -DEPENDENT ON POTENTIAL COVID-19 DELAYS	+ CHF 3.0
Q1	EVENAMIDE	SCHIZOPHRENIA	PHASE IIB/III	START OF POTENTIALLY PIVOTAL PHASE III TRIAL IN SCHIZOPHRENIA PATIENTS (MAJOR INDICATION) - DEPENDENT ON POTENTIAL COVID-19 DELAYS	+ CHF 13.4

* PD-LID = PARKINSON'S DISEASE LEVODOPA-INDUCED DYSKINESIA; ** CTRS = CLOZAPINE TREATMENT-RESISTANT SCHIZOPHRENIA

ESTIMATES AS OF 5 MAY 2021

SOURCE: VALUATIONLAB ESTIMATES, NEWRON PHARMACEUTICALS

Key catalysts:

- **Results evenamide FDA explanatory safety "Study 008A" (end 2021):** with 30 mg BID therapeutic evenamide dose - required by the FDA to address concerns of CNS events seen in animals before starting pivotal trials in schizophrenia and CTRS.
- **Start potentially pivotal program of evenamide in schizophrenia/CTRS (Q1 2022):** Our rNPV for evenamide in schizophrenia/CTRS jumps by CHF 16.4/share with a 50% (potentially pivotal) success rate from currently CHF 7.0/share with a 15% (POC) success rate.
- **Start new label trial Xadago in PD-LID (Q1 2022):** Our rNPV for Xadago in PD-LID rises by CHF 1.3/share with a 65% (phase III) success rate from currently CHF 0.4/share with a 15% (proof-of-concept - POC) success rate.

Technology & Pipeline

Search & Development company focused on CNS and orphan diseases
Newron has two drugs addressing multibillion-dollar markets including Xadago (Parkinson's disease) and evenamide (schizophrenia), with each drug addressing an orphan-like indication, PD-LID with Xadago and CTRS with evenamide.

PRODUCT PIPELINE

PRODUCT	DRUG CLASS	INDICATION	STATUS	LAUNCH DATE (EXPECTED)	PARTNER	PEAK SALES
XADAGO (SAFINAMIDE)	ALPHA-AMINOAMIDE	PARKINSON'S DISEASE (MAJOR INDICATION)	EU: LAUNCHED US: APPROVED	EU: H1 2015 US: JULY 2017	ZAMBON/MEIJI SEIKA/ EISAI/SUPERNUS PHARMA	EUR 200+ MN
XADAGO (SAFINAMIDE)	ALPHA-AMINOAMIDE	LEVADOPA-INDUCED DYSKINESIA (ORPHAN INDICATION)	PIVOTAL TRIAL (START H2 2021)	2024	ZAMBON/MEIJI SEIKA/ EISAI/SUPERNUS PHARMA	EUR 200 MN
EVENAMIDE	ION CHANNEL BLOCKER	SCHIZOPHRENIA (MAJOR INDICATION)	PIVOTAL TRIAL (START Q3 2021)	2025	PARTNER AFTER PIVOTAL TRIAL	EUR 1+ BN
EVENAMIDE	ION CHANNEL BLOCKER	CLOZAPINE TREATMENT-RESISTANT SCHIZOPHRENIA (ORPHAN INDICATION)	PIVOTAL TRIAL (START Q3 2021)	2024	PARTNER AFTER PIVOTAL TRIAL	EUR 100+ MN
RALFINAMIDE	ION CHANNEL BLOCKER	NON-RESPONDING SEVERE NEUROPATHIC PAIN (ORPHAN INDICATION)	POC*		PARTNER AHEAD OF TRIALS	NON-CORE

* POC = PROOF-OF-CONCEPT
ESTIMATES AS OF 5 MAY 2021
SOURCE: VALUATIONLAB ESTIMATES, NEWRON PHARMACEUTICALS

Xadago generating product sales in the EU and the US with more to come
Germany was the first EU member state to launch Xadago in May 2015. The European roll out of Xadago is well on its way, with Xadago now available in more than 15 European countries and more country launches to follow. In March 2017, Xadago received US approval, triggering a EUR 11.3 mn milestone payment from Zambon. The US specialty pharmaceutical company US WorldMeds launched Xadago in the US in July 2017. In June 2020, Supernus Pharma acquired the US commercialization rights to Xadago after it acquired the CNS portfolio of US WorldMeds. This may provide an incentive for an improved sales push. Additionally, Zambon and its regional partners have gained approval for Xadago in Australia, Canada, Brazil and Columbia. Additional distribution agreements in Southern Europe, the Middle East, Africa and South America are underway. Partner Meiji Seika, together with Eisai, received Japanese approval in September 2019 where the drug is branded Equfina. In Q1 2022, the single, potentially pivotal label extension trial of Xadago in PD-LID should start, which could add EUR 200 mn peak sales to our Xadago forecasts.

Evenamide pivotal trials in schizophrenia and CTRS to start in Q1 2022
With sufficient cash secured and the setback of sarizotan in Rett syndrome, Newron has stepped up its development plans for evenamide in schizophrenia and CTRS. Pivotal development is expected to start in Q1 2022 after addressing the safety concerns seen in animals flagged by the FDA in May 2019, with the final safety and efficacy “Study 008A” expected to report by end 2021.

Non-core projects are up for partnering or to be monetized
Ralfinamide (neuropathic pain), a pipeline project stemming from Newron’s own ion channel blocker discovery platform, is considered non-core that the company wants to partner or monetize.

CNS and orphan diseases a good mix for a small biopharmaceutical company
Newron’s development programs are primarily focused on new generation ion channel blockers for the treatment of CNS-related diseases and pain. With existing treatments for CNS disorders lacking efficacy, tolerability and long-term safety, demand is set to rise as the population ages. This is an attractive market opportunity for a small, specialized

biopharmaceutical company. Moreover, many large pharmaceutical companies have withdrawn from this field due to clinical setbacks and the high risks involved.

Strategy to complement CNS portfolio with rare disease opportunities
Newron plans to seek new orphan drug opportunities, after the termination of sarizotan in Rett syndrome in 2020, to replenish its development pipeline.

Regulatory authorities provide incentives to develop drugs for rare diseases
Orphan diseases are life-threatening or chronically debilitating diseases with an incidence less than 1 per 2,000/5,000 people. Although individually, orphan diseases may be classified as rare, collectively, they affect a large portion of the population and health care expenditure. The US and EU orphan disease programs have been developed to provide pharmaceutical companies a strong incentive to pursue and develop orphan prescription drugs for these less common disorders.

Key advantages for orphan drugs include:
- High unmet medical need for a relatively small patient population
- Strong orphan disease market exclusivity of 7 years (US) or 10 years (EU) starting from first day of launch – this provides sufficient time for an attractive return
- Competition is not present or limited
- Faster speed to market, lower development costs, lower regulatory hurdles
- Higher selling prices and profit margins
- Specialists can be addressed by a relatively small sales force

However, there are also considerable hurdles, including:
- Insufficient understanding of the history or mechanism of disease
- A very low number of patients to conduct clinical trials – lack of robust clinical data, slow enrollment, study delays
- A lack of widespread expertise in clinical centers
- Absence of a clear regulatory pathway on how to set up the pivotal clinical trial, including what the right endpoints should be
- The small number of experts who conduct the trials are often banned from advisory panels – they are considered to have a conflict in interest

Renewed interest in orphan drugs with attractive partnering opportunities
Orphan indications typically carry a high development risk. However, the low development costs and fast development times mitigate the financial impact and therefore are quite suitable for small, specialized biopharmaceutical companies to pursue. Many patient organizations provide valuable (financial) support. In the past, Big Pharma largely discarded orphan indications. Now there seems to be a renewed interest, with Big Pharma desperately seeking new profitable revenue streams to replenish their product portfolios affected by patent expirations. This provides Newron additional partnering opportunities for its emerging pipeline of orphan drugs, next to mid-sized specialty pharmaceutical companies.

In the following section we provide an in-depth analysis for Newron's key drivers including:
- **Evenamide as an add-on therapy for schizophrenia/CTRS** (page 18)
- **Xadago in Parkinson's disease/PD-LID** (page 33)

Forecasts & Sensitivity Analysis

Evenamide (schizophrenia)

Product Analysis

Evenamide all indications: peak sales EUR 1.2+ bn, rNPV CHF 7.0/share

1) Schizophrenia peak sales of EUR 1.1 bn - rNPV of CHF 5.7 per share

We forecast peak sales of EUR 1.1 bn for evenamide in its major indication as an add-on to existing schizophrenia therapies, assuming Newron starts two cross-supportive potentially pivotal trials, "Study 003" in schizophrenia and "Study 004" in the orphan indication CTRS (clozapine treatment-resistant schizophrenia) in Q1 2022 after successfully completing "Study 008A" by end 2021 to fully address the FDA safety concerns. Topline results are expected in Q3 2023. Following positive "Study 008A" results, we assume Newron to sign on a major CNS player to fully develop and commercialize evenamide in schizophrenia and potentially other CNS disorders such as mania or depression. We expect first launches in schizophrenia to occur in early 2025 and global patent protection until 2033 (including patent term extensions), 10-years data exclusivity on approval in the EU (2035), a conservative daily treatment cost of between USD 15 (US) and EUR 10 (EU/ROW), and a target market penetration peaking at ~15% (EU/ROW) and ~20% (US). Our rNPV amounts to CHF 102 mn, or CHF 5.7 per share, assuming Newron receives a total of EUR 273 mn of upfront and milestone payments, royalties on sales of 20% from its partner(s) with a success probability of 15% (POC completed) and a WACC of 7% (for details see page 28).

2) CTRS peak sales of EUR 100+ mn – rNPV of CHF 1.3 per share

The orphan-like indication CTRS (clozapine treatment-resistant schizophrenia) triggered the fast-to-market development plans for evenamide. Although, CTRS is a niche market, its high unmet medical need makes evenamide eligible for orphan and fast track designation, where a single potentially pivotal trial is required for approval, which can be combined with a single potentially pivotal trial in schizophrenia. We expect the pivotal CTRS trial to start in Q1 2022 with topline results due in Q3 2023 and launch in 2024 due to priority review. We conservatively forecast peak sales to amount to EUR 132 mn assuming the same pricing as for schizophrenia. We calculate a rNPV of CHF 23 mn or CHF 1.3 per share assuming Newron commercializes evenamide in CTRS in the US through an own small specialist sales force, and out licenses the drug in CTRS outside the US to the same partners as for schizophrenia with the same 20% royalty rate with EUR 25 mn milestone payments with a 15% (proof-of-concept) success rate (for details see page 29).

NOTE: Our success rate for evenamide in schizophrenia and CTRS will increase to 50% when the pivotal phase III trials start in Q1 2022. Consequently, our rNPV for evenamide in schizophrenia/CTRS will jump by CHF 16.4 per share from currently CHF 7.0 per share. Our pricing could prove conservative if evenamide provides a new treatment paradigm in schizophrenia with annual pricing up to USD 10-15,000 per patient in the US.

Pivotal plan for evenamide provides substantial upside and speed

Newron has come up with a development plan for evenamide that can speed up development and approval based on the positive POC data for evenamide in schizophrenia

announced at the beginning of 2017 and new insights into the orphan indication CTRS (clozapine treatment-related schizophrenia). After active consultations with key opinion leaders and regulators, the company has completed discussions with the EMA's CHMP and FDA to start parallel development of evenamide in its major indication schizophrenia and the orphan indication CTRS with a single, potentially pivotal, phase III trial for each indication that will be cross-supportive for approval. CTRS provides a fast-to-market opportunity for evenamide being an orphan indication with the potential for shorter development timelines, lower development costs and an expedited review.

Funding secured to partner late, but Newron may partner or co-develop to reduce risk
We believe Newron has secured sufficient funding for the pivotal development of evenamide in both indications through a successful CHF 27 mn capital increase in September 2017 and two remaining tranches worth EUR 15 mn from the EUR 40 mn EIB loan facility in October 2018. Newron is currently evaluating potential options for partnering or co-developing the further development of evenamide in schizophrenia and other related indications such as mania or depression. We assume the company to sign a (co)development and commercialization agreement with a major CNS player shortly after successfully completing the safety and efficacy "Study 008A" trial by end 2021, for substantial upfront, regulatory and commercial milestones and royalties on sales, further strengthening their cash position. Newron plans to establish an own small specialist sale force to commercialize evenamide in CTRS orphan indication in the lucrative US market to optimize its long-term value.

Start of the two pivotal evenamide trials delayed by FDA due to safety concerns
Newron originally wanted to start both pivotal trials for evenamide in schizophrenia and CTRS in 2019. Unfortunately, in May 2019 the FDA signaled potential chronic toxicity concerns with evenamide in a study in rats as well as CNS (central nervous system) events at high doses in a study with dogs, with the potential implication of these findings for patients. The FDA requested Newron to delay the start of both pivotal trials until additional short-term explanatory studies in rats and humans adequately addressed these concerns. All the evenamide pre-clinical trials requested by the FDA have now been completed with no toxicity concerns identified. The CNS events appear to be a known "class effect" with sodium channel blockers in animal studies, which also occurred with Xadago and were ultimately resolved.

Short-term explanatory studies required by FDA underline favorable safety profile
In April 2021, Newron announced the initial results from the two short-term explanatory studies in evenamide required by the FDA before starting the phase III program in schizophrenia. Both "Study 010" in healthy volunteers and "Study 008" in patients with schizophrenia met the primary objective of safety and efficacy on all safety variables. Data from "Study 008" is a key component in the data package submitted to the FDA to support approval to start Newron's pivotal phase III trial program for evenamide in schizophrenia. Preclinical results confirming absence of toxicity were already submitted to the FDA to support this data package.

1. **"Study 010" shows no increased risk of QTc prolongation or arrhythmias**
   "Study 010" is a four-week, single dose, cross-over Thorough QT (TQT) study in 56 healthy volunteers, was designed to evaluate the effects of evenamide 30 mg and 60 mg (twice the therapeutic dose), compared to placebo and the antibiotic moxifloxacin 400 mg on the QT segment specifically, and on the electrocardiogram (ECG) generally, as requested by the FDA and under the International Council for

Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH). The results indicate that evenamide was devoid of any QTcF prolongation compared to placebo (indicating lack of any increased risk of arrythmia), while moxifloxacin was associated with a 17.3 ms median maximum increase suggestive of clinically significant risk of arrhythmia. These results strongly suggest that evenamide does not increase a patient's risk of QTc prolongation and arrhythmias, a risk generally associated with antipsychotics.

2. **"Study 008" shows no symptoms suggestive of severe CNS events or seizures**
"Study 008" is a four-week, randomized, double-blind placebo-controlled study was designed to primarily evaluate the safety, tolerability, and electroencephalogram (EEG) effects of two fixed doses of evenamide, 7.5 mg and 15 mg BID (twice daily). The study was requested by the FDA to address questions which arose from a study of evenamide in rats, and central nervous system (CNS) events observed following high-dose administration of evenamide in dogs. "Study 008" was performed in 138 outpatients with chronic schizophrenia, receiving treatment with a second-generation atypical antipsychotic at study centers in the US and India. Over 95% of the patients completed the study. No patient on evenamide discontinued from the study due to adverse events, and there were no significant adverse events relating to evenamide. No symptoms were observed suggestive of severe CNS events, symptoms/signs of seizures, EEG diagnosis of seizure-like activity, or cardiac events in patients with evenamide. There were no differences in laboratory, ECG or vital signs abnormalities between evenamide and placebo-treated patients. The most frequent adverse events observed were related to CNS, gastrointestinal disorders, psychiatric disorders, metabolism and nutrition disorders and laboratory investigations. The most frequent adverse events reported (greater than 5%) were headache and somnolence, which were equally distributed between evenamide and placebo.

"Study 008" was designed to primarily assess safety and was not powered to demonstrate efficacy. The 7.5 mg BID was a "no-effect" dose, which will not be investigated further as expected. The 15 mg BID dose showed a higher response on the total PANSS than 7.5 mg BID, however, this was not statistically significant when compared to placebo.

A final "Study 008A" trial required by the FDA is expected to complete by end 2021
The safety of the 30 mg BID therapeutic dose of evenamide will be assessed in an additional safety and efficacy "Study 008A" trial in patients with schizophrenia, to fully comply with the FDA's original request prior to starting the phase III program. "Study 008A" will start in May with results expected by end 2021. Following positive "Study 008A" results, the phase III program for evenamide in schizophrenia is expected to start in Q1 2022.

Newron confident to start the two pivotal schizophrenia trials in Q1 2022
Consequently, Newron is confident it can start the two pivotal trials of evenamide in schizophrenia and CTRS in Q1 2022. Each trial is expected to complete in 18 months with topline data expected in Q3 2023. Next to these two trials, Newron plans to start a compassionate use program in CTRS to gather sufficient safety data required for expedited approval.

Targeting a USD 12 bn antipsychotic market with a major and orphan indication

Evenamide stems from Newron's own ion channel discovery efforts and has shown benefit in a range of models of positive symptoms, aggression, cognition (in schizophrenia), mania, depression and obsessive behavior. This novel, small molecule, oral drug has a rapid onset of action and has a high availability in the brain. Evenamide targets a large antipsychotic market worth approximately USD 12 bn currently affected by several branded drugs losing patent protection. The drug can be added to current antipsychotic therapy for patients who no longer respond (roughly 65% of patients). In 2017, Newron successfully completed a phase IIa POC trial of evenamide in schizophrenia. Evenamide enjoys an extensive patent life running until at least 2033 (including 5 years patent term extension), thanks to the US Patent and Trade Organization that granted a solid composition of matter patent in 2013. Assuming evenamide receives orphan drug designation for CTRS, the compound is eligible for 7 and 10-years orphan drug market exclusivity upon approval in the US and EU, respectively.

Evenamide targets a USD 6 bn schizophrenia market in need of new treatments

Evenamide is being developed as an add-on therapy to current antipsychotic medication for schizophrenia patients who respond poorly, including CTRS patients that is considered an orphan indication. The schizophrenia market is currently worth approximately USD 6 bn, despite low patient compliance and many patients responding poorly to current antipsychotic therapy. Evenamide would become a first-in-class voltage gated, selective sodium channel blocker specifically developed as an add-on to existing treatments for schizophrenia and CTRS. Therefore, the drug has the potential to be developed in fixed-dose combinations with existing treatments extending their patent life substantially.

Positive POC results demonstrate unique profile as schizophrenia add-on therapy

In January 2017 Newron reported positive headline results of the phase IIa POC trial of evenamide in schizophrenia. Detailed results of the POC trial were presented at the International Congress on Schizophrenia Research (ICSR) annual meeting at the end of March. Evenamide met the trial objectives of good tolerability, safety and showed preliminary evidence of efficacy.

Rigorous POC trial protocol finalized with FDA input and guidance

The 4-week, double blind, placebo-controlled, randomized, multinational POC trial was designed to assess the safety, tolerability and early evidence of efficacy of evenamide as an add-on treatment in 89 patients with a diagnosis of schizophrenia. The trial protocol, including doses and trial design, was finalized with FDA input and guidance, and was approved by the Indian regulator DCGI (Drug Controller General of India). Patients included in the trial were mostly male (86%) between 19 and 60 years of age, with a mean baseline PANSS (Positive And Negative Syndrome Scale) total score of 62.9 ± 7.4, and were experiencing breakthrough psychotic symptoms while on stable and adequate doses of mainstay schizophrenia treatments such as JNJ's Risperdal (risperidone) (mean dose: 4.2 ± 2.0 mg/day; n=70) or Lundbeck's Abilify (aripiprazole) (mean dose: 19.7 ± 7.0 mg/day; n=19), the atypical antipsychotics to which they had responded previously. The trial was conducted in two US (61 patients) and three Indian (28 patients) centers, which enrolled patients with schizophrenia with a mean duration of illness of approximately 18 years and an average of three hospitalizations. Patients were randomized to receive evenamide twice daily (15-25 mg) or placebo on top of their current antipsychotics.

Well tolerated on top of mainstay schizophrenia treatments

Evenamide, given 15-25 mg twice daily, was generally well tolerated in the POC trial, with no meaningful differences between groups in changes from baseline in vital signs, laboratory test results or ECG findings.

As can be seen in the table below, 5 (10%) patients had at least one serious adverse event (SAE) vs. 1 (2.6%) in the placebo group. Two adverse events (atrial fibrillation and seizure) were reported as a SAE. In the patient with atrial fibrillation, the highest concentration of evenamide was ~11-18 fold less than that producing cardiac events in animals. In the patient experiencing a seizure, the highest plasma concentration was ~16-40 fold less than that associated with seizures in animals. Treatment of evenamide in these two patients (3%) was discontinued.

ADVERSE EVENTS (>5% OF PATIENTS)	EVENAMIDE (N=50) N (%)	PLACEBO (N=39 N (%)	TOTAL (N=89) N (%)
AT LEAST ONE SAE (SERIOUS ADVERSE EVENT)	5 (10.0%)	1 (2.6%)	6 (6.7%)
AT LEAST ON TEAE (TREATMENT EMERGENT ADVERSE EVENT)	23 (46.0%)	12 (30.8%)	35 (39.3%)
SOMNOLENCE (STRONG DESIRE TO SLEEP)	8 (16.0%)	5 (12.8%)	13 (14.6%)
INSOMNIA (TROUBLE SLEEPING)	5 (10.0%) *	1 (2.6%)	6 (6.7%)
HEADACHE	3 (6.0%) **	0	3 (3.4%)
OVERDOSE	3 (6.0%)	1 (2.6%)	4 (4.5%)
DRY MOUTH	3 (6.0%)	2 (5.1%)	5 (5.6%)
DIARRHEA	0	2 (5.1%)	2 (2.2%)
PAIN IN EXTREMITY	0	3 (7.7%)	3 (3.4%)
ADVERSE EVENTS (ALL)	EVENAMIDE	PLACEBO	TOTAL
ADVERSE EVENTS (SERIOUS SEVERITY)	2 OF 69 (3%)	0 0F 34 (3%)	2 OF 103 (2%)
ADVERSE EVENTS (MILD SEVERITY)	58 OF 69 (84%)	30 OF 34 (88%)	88 0F 103 (85%)
ADVERSE EVENTS (MODERATE SEVERITY)	9 OF 69 (13%)	4 0F 34 (12%)	13 OF 103 (13%)

* 1 PATIENT QUALIFIED AS MODERATE SEVERITY; ** 2 PATIENTS QUALIFIED AS MODERATE SEVERITY

SOURCE: VALUATIONLAB, NEWRON PHARMACEUTICALS

Most adverse events were of mild severity for evenamide (84%) and placebo (88%), while 13% of adverse events in the evenamide group were qualified as moderate compared to 12% on placebo. The evenamide group had a higher incidence of somnolence (strong desire to sleep), insomnia (trouble sleeping), headache, overdose and dry mouth than placebo. Placebo had a higher incidence in diarrhea and pain in extremities compared to the evenamide group.

The proportions of patients with clinically notable abnormalities in vital signs or laboratory values were very low and were similar in the evenamide and placebo groups. The proportion of patients with clinically significant ECG abnormalities was low and similar between groups, and there was no evidence of effects on QTc prolongation (a risk factor for sudden death). Assessment of extrapyramidal symptoms (EPS) using the Extrapyramidal Symptoms Rating Scale did not reveal any treatment-emergent EPS with evenamide treatment.

Promising early efficacy in improving the symptoms of schizophrenia

The results of the POC trial showed a benefit on all measures assessed. Patients treated with evenamide showed improvement on the symptoms of schizophrenia assessed by the Positive and Negative Syndrome Scale (PANSS). The PANSS is a widely used medical scale for measuring symptom severity of patients with schizophrenia, including positive

BASELINE VALUE AND MEAN CHANGE FROM BASELINE AT DAY 28 (MITT POPULATION)

	BASELINE VALUE				CHANGE FROM BASELINE TO DAY 28			
	EVENAMIDE (N=44)		PLACEBO (N=39)		EVENAMIDE (N=44)		PLACEBO (N=39)	
SCALE	N	MEAN (SD)	N	MEAN (SD)	N	MEAN (SD)	N	MEAN (SD)
PANNS TOTAL (SYMPTOM SEVERITY)	47	57.8 (9.66)	39	59.3 (10.81)	47	-5.1 (9.67)	39	-3.7 (9.65)
LOF TOTAL (PATIENTS' FUNCTIONING)	48	22.04 (3.608)	39	20.64 (4.533)	48	0.72 (3.321)	39	0.31 (3.130)
CGI-S (SEVERITY OF ILLNESS)	47	3.1 (0.68)	39	3.2 (0.77)	47	-0.3 (0.60)	39	-0.2 (0.74)

SOURCE: VALUATIONLAB, NEWRON PHARMACEUTICALS

symptoms, which refer to an excess or distortion of normal functions (e.g. hallucinations and delusions) and negative symptoms, which represent a diminution or loss of normal functions (e.g. emotional or social withdrawal).
As can be seen in the table above, the mean change from baseline at day 28 for the **PANSS Total score** in the mITT (modified intent to treat) population was greater for evenamide at -5.1 than for placebo at -3.7 (a reduction in score represents an improvement). Numerically greater improvement with evenamide was also observed for patients' functioning with the Strauss-Carpenter **Level of Functioning (LOF) Total scale** (an increase in score represents an improvement); and severity of illness with the Clinical **Global Impression of Severity (CGI-S) score** (a reduction in score represents an improvement), compared to the standard antipsychotic alone.

As can be seen in the following table, for the PANSS Positive Symptoms sub-scale, a statistically significant/near significant improvement from baseline (mean baseline score: 14.8 ± 2.8) to day 28 for evenamide, compared to placebo [LS mean difference (SE)], was noted in the: **1) MMRM** (Mixed-Effect Model Repeated Measure) model [-1.19 (0.643), p=0.0678]; **2) ANCOVA-LOCF** (Analysis of Covariance - Last Observation Carried Forward) [-1.28 (0.632), p=0.0459]; and **3) ANCOVA-OC** (Analysis of Covariance – Observed Cases) [-1.48 (0.641), p=0.0237] analyses.

PANNS POSITIVE SCALE TOTAL SCORE: MEAN CHANGE FROM BASELINE (MITT POPULATION)

	CHANGE FROM BASELINE				DIFFERENCE EVENAMIDE VS. PLACEBO		
	EVENAMIDE (N=44)		PLACEBO (N=39)				
DAY 28	N	LS MEAN (SE)	N	LS MEAN (SE)	LS MEAN (SE)	(95% CI)	P-VALUE
MMRM	47	-2.06 (0.439)	39	-0.87 (0.643)	-1.19 (0.643)	(-2.47, 0.09)	0.0678
ANCOVA (LOCF)	48	-2.31 (0.445)	39	-1.03 (0.477)	-1.28 (0.632)	(-2.54, -0.02)	0.0459
ANCOVA (OC)	43	-2.51 (0.454)	39	-1.03 (0.475)	-1.48 (0.641)	(-2.76, -0.20)	0.0237

SOURCE: VALUATIONLAB, NEWRON PHARMACEUTICALS

In addition, a global assessment of change from baseline in the patient's overall condition **Clinical Global Impression of Change (CGI-C)**, performed by a clinician, showed a greater proportion (p=0.084; Fisher's exact chi-square test) of evenamide-treated patients rated as improved (54.2%), compared to placebo (35.9%). An improvement was qualified as a rating of 1 (very much improved), 2 (much improved) or 3 (minimally improved).

PROPORTION OF RESPONDERS AT DAY 28

SCALE	RESPONDER CRITERIA	N	EVENAMIDE	N	PLACEBO
PANSS POSITIVE (SYMPTOM IMPROVEMENT)	CHANGE FROM BASELINE LESS THAN 0 (REDUCTION IN SCORE = IMPROVEMENT)	50	35 OF 47 (74.5%) *	39	17 OF 39 (43.6%)
CGI-C (PATIENT'S OVERALL	RATING OF 1 (VERY MUCH IMPROVED), 2 (MUCH IMPROVED) OR 3 (MINIMALLY IMPROVED)	50	26 OF 47 (55.3%) **	39	14 OF 39 (35.9%)

* P-VALUE < 0.05 VS. PLACEBO, FISCHER'S EXACT CHI-SQUARE TEST; ** P < 0.1 VS. PLACEBO

SOURCE: VALUATIONLAB, NEWRON PHARMACEUTICALS

An additional analysis demonstrated that the proportion of patients who showed improvement on the **PANSS Positive sub-scale** at day 28 was significantly greater (p=0.0043; Fisher's exact chi-square test) for the evenamide group (74.5%) compared to the placebo group (43.6%). An improvement was qualified in the PANSS Positive score as a change from baseline less than zero (note: a reduction in score is an improvement).

Finally, results indicate that patients who were younger (less than 32 years of age) and earlier in the course of their disease (less than 10 years) experienced greater improvement.

The results from the small POC trial are consistent with the hypothesis that evenamide as an add-on to current antipsychotic treatment will improve symptoms of psychosis in patients

who no longer respond adequately to standard antipsychotic treatment. The POC trial would suggest that evenamide could be added to the treatment regimen to enhance response, instead of switching the treatment regimen with another, which leads to discontinuation effects, anti-dopaminergic, metabolic and sexual side effects or the need to hospitalize patients.

CTRS provides fast-to-market opportunity, orphan drug exclusivity, own sales effort
CTRS affects approximately 21,000 patients in the US and an estimated 45,000 patients in the EU/ROW and is therefore considered an orphan indication. Although CTRS represents only a small niche opportunity for evenamide (conservatively assuming similar pricing as for schizophrenia), it provides major benefits, including:

- Fast-to-market opportunity (orphan indication with shorter development time, lower development costs, expedited review)
- 7-years (US) and 10-years (EU) orphan drug exclusivity upon approval
- Potential for parallel development of evenamide in schizophrenia (cutting 2-3 years development time)
- Potential for Newron to market evenamide in CTRS through an own small specialist sales force in the US where most patients are institutionalized

Up to 30% of people with schizophrenia do not respond to two (or more) treatments of second-generation dopaminergic antipsychotics and are said to have treatment-resistant schizophrenia, which typically develops after 3-5 years of treatment. 10-20% of patients already show symptoms of resistance in the first period of treatment. These patients continue to be psychotic with unresolved symptoms such as delusions, hallucinations, social withdrawal, hostility, grandiosity, and cognitive impairment. Treatment-resistant schizophrenia has a high morbidity (e.g. hospitalization) and mortality rate (e.g. suicide) with some of the highest rates of hospitalization and costs to society with an estimated USD 34 bn in direct healthcare costs in the US alone.

30% of treatment-resistant schizophrenia patients fail clozapine treatment
Clozapine, a dopamine and serotonin antagonist (5HT2A) that was first introduced in the 1960's with a few unique differences compared to other second-generation dopaminergic antipsychotics, is still the only effective treatment for treatment-resistant schizophrenia. It is the only drug with an FDA indication for treatment-resistant schizophrenia and reducing suicidal behavior. No drug other than clozapine has shown efficacy in these patients or a reduction of suicide attempt. Unfortunately, 30% of treatment-resistant schizophrenia patients on clozapine do not respond adequately or develop resistance to its effects and are defined as clozapine treatment-resistant schizophrenia (CTRS) patients. These patients have no other treatment options, with an estimated 80% of patients in the US institutionalized in selected Veteran Affairs, state, city hospitals and prison system. A similar prevalence is estimated for the EU, Japan and Canada.

Glutamate system appears to be involved with treatment-resistant schizophrenia
Studies suggest treatment-resistant schizophrenia may be differentiated by abnormalities in brain glutamate concentrations not seen in treatment-responsive schizophrenia patients. This suggests a categorical difference rather than one of severity, indicating treatment-resistant schizophrenia is a different kind of illness than treatment-responsive schizophrenia. Interestingly, case studies, small placebo-controlled trials and meta-analyses

suggest a benefit of the anticonvulsant drug lamotrigine (branded Lamictal by GlaxoSmithKline) as add-on treatment in CTRS, albeit with considerable variability among trials. Lamotrigine is a member of the sodium channel blocking class of antiepileptic drugs, which suppress the release of glutamate and aspartate, two of the dominant excitatory neurotransmitters in the central nervous system. The benefits of lamotrigine are most likely due to the suppression of glutamate release.

Evenamide antagonizes (in vivo): 1) the effect of ketamine (a glutamate antagonist) on PPI, and 2) effects of MK-801 and PCP (glutamate releasers). In animal models of schizophrenia, evenamide mimics effects of clozapine. However, clozapine does not reduce glutamate while evenamide does, making it an attractive add-on treatment for CTRS patients.

Next steps: start two cross-supportive pivotal trials in schizophrenia and CTRS
Based on the positive findings of the POC trial, and new insights into the potential of evenamide in CTRS, Newron has completed meetings with regulatory authorities and finalized the potentially pivotal trial designs for development of evenamide in its two targeted indications, consisting of:

1. **"Study 003" in schizophrenia (major indication):** an international, double-blind placebo-controlled potentially pivotal phase IIb/III trial in ~30 centers of three fixed doses of evenamide (7.5, 15 or 30 mg twice-daily) or placebo as an add-on to atypical antipsychotics in 520 patients (130/group) experiencing worsening of symptoms of schizophrenia with a treatment duration of 6 weeks, primary endpoint is the PANSS Total Score, normal review; estimated 18 months to completion with a cost of EUR ~20 mn
2. **"Study 004" in CTRS (orphan indication):** an international, double-blind, placebo-controlled potentially pivotal phase III trial with two doses of evenamide (15 or 30 mg twice-daily) or placebo as an add-on therapy in 450 (150/group) treatment-resistant schizophrenia patients not responding adequately to clozapine with a treatment duration of 8 weeks, clozapine levels will be measured at baseline while patient compliance will be monitored by patients sending photos taking their medication, primary endpoint is the PANSS Total Score, expedited review; estimated 18 months to completion with a cost of EUR ~10 mn

Both phase IIb/III trials will be followed by separate extension trials to evaluate long-term efficacy, safety and tolerability. Patients who have completed "Study 003" will be invited to enroll in an extension trial "Study 005" where they will continue double-blind treatment on the same dose for an additional 46 weeks, while patients who have completed "Study 004" will be enrolled in "Study 006" where all patients will have evenamide dose titrated to remain blinded for an additional 44 weeks.

Two cross-supportive pivotal phase III trials of evenamide to start in Q1 2022
Newron is confident it will fully resolve the FDA safety concerns by completing safety and efficacy "Study 008A" with the 30 mg BID therapeutic dose of evenamide in schizophrenia patients by end 2021 and shortly thereafter start the two pivotal trials in Q1 2022. Top line results are expected in Q3 2023 and intended to be cross-supportive for approval of evenamide in both indications. If "Study 003" and "Study 004" are both positive, then evenamide should be approved in both indications; if only "Study 004" is positive, then evenamide will receive an accelerated approval in CTRS; if only "Study 004" is positive, then a second confirmatory phase III trial will be required for approval of evenamide in

schizophrenia. Newron expects to start expanded access and compassionate use programs in treatment-resistant schizophrenia patients to add to the safety database required for approval once the pivotal trials start.

Evenamide has global peak sales potential of EUR 1.2+ bn

To correctly reflect and value Newron's plans to develop evenamide in two indications, a major indication schizophrenia and an orphan indication CTRS, we have made separate forecasts for each indication.

1) Schizophrenia (major indication) peak sales potential of EUR 1.1+ bn

Worldwide there are more than 21 mn people suffering from schizophrenia, of which more than 2 mn are in the US, and around 5 mn in the EU, Japan and Australia. These are the major markets for evenamide. Roughly 70% of schizophrenia patients experience positive symptoms and are treated with typical and atypical antipsychotics, of which only 25% of patients is on treatment due to poor patient compliance. This is the main target population where evenamide will be used as an add-on for standard schizophrenia treatment. Evenamide could potentially lead to higher patient compliance and less switching of antipsychotic therapy due to patients responding longer to the combination therapy, providing substantial upside to our forecasts in schizophrenia.

In our forecasts we assume Newron will out license evenamide on positive safety and efficacy "Study 008A" trial results expected by end 2021 to a strong CNS player in return for substantial upfront, development and sales milestone payments and 20% royalties on sales. First launches in schizophrenia are expected in early 2025.

In our detailed evenamide forecasts we have accounted for two major regions, namely:

1) **Europe/ROW:** we forecast peak sales to amount to EUR 577 mn assuming a conservative daily treatment price of EUR 10, 10 years data exclusivity, and a peak penetration rate amounting to ~15%. We assume total milestone payments to amount to EUR 130 mn.
2) **US:** peak sales could amount to around EUR 491 mn assuming a conservative daily treatment price of USD 15, patent protection until 2033 (including 5 years patent term extension), and a peak penetration rate amounting to ~20%. We assume total milestone payments of EUR 143 mn.

2) CTRS (orphan-like indication) peak sales potential of EUR 100+ mn

Of the treatment-resistant schizophrenia patients approximately 12% are treated with clozapine, which is the target population for evenamide where it will be used as an add-on to clozapine. We expect high peak market penetration rates due to the severity of the illness and lack of alternative medications. We conservatively assume similar pricing in CTRS as for schizophrenia. Higher "orphan drug" pricing could lead to considerable upside to our forecasts. First launches are expected in 2024. We assume Newron will commercialize evenamide in CTRS in the US through an own small specialist sales force. Outside the US, we expect Newron to out license CTRS rights to the same commercialization partners as for schizophrenia with 20% sales royalties and upfront and commercialization milestone payments.

1) **Europe/ROW:** we forecast peak sales to amount to EUR 74 mn assuming a conservative daily treatment price of EUR 10, 10 years orphan drug exclusivity, and

a peak penetration rate amounting to ~40%. We assume total milestone payments to amount to EUR 25 mn.

2) **US:** peak sales could amount to around EUR 60 mn assuming a conservative daily treatment price of USD 15, patent protection until 2033 (including 5 years patent term extension), and a peak penetration rate amounting to ~50%. We account for the buildup of a small specialist sales force and assume COGS to amount to 15% of sales.

Our detailed forecasts and sensitivity analysis for schizophrenia and CTRS can be seen on the following two pages.

NOTE: Evenamide's potential could be substantially larger than our forecasts given the size of the market, additional indications such as depression or mania.

Forecasts & Sensitivity Analysis

Schizophrenia (major indication)

EVENAMIDE - FINANCIAL FORECASTS FOR SCHIZOPHRENIA

INDICATION	ADD-ON THERAPY TO ANTIPSYCHOTICS FOR REDUCING POSITIVE SYPMTOMS AND PSYCHOTIC WORSENING IN PATIENTS WITH SCHIZOPHRENIA
DOSAGE	15-25 MG TWICE DAILY (TBD)
PRICE	USA: USD 15/DAY, EU/ROW: EUR 10/DAY; PRICING MAY PROVE CONSERVATIVE IF EVENAMIDE BECOMES A NEW TREATMENT PARADIGM IN SCHIZOPHRENIA
STANDARD OF CARE	ATYPICAL (2ND GENERATION) ANTIPSYCHOTICS SUCH AS ZYPREXA, SEROQUEL, RISPERDAL, GEODON, ABILIFY
UNIQUE SELLING POINT	FIRST ADD-ON TO MAINSTAY ANTIPSYCHOTIC THERAPY FOR SCHIZOPHRENIA WITH THE POTENTIAL TO PROLONG RESPONSE RATES AND REDUCE FREQUENT SWITCHING
7Ps ANALYSIS	
PATENT	US: PROTECTION UNTIL 2033 BASED ON COMPOSITION OF MATTER PATENT GRANTED UNTIL 2028 + 5 YEARS EXTENSION; EU: 10-YEARS DATA EXCLUSIVITY
PHASE	POSITIVE POC RESULTS AS ADD-ON THERAPY TO ANTIPSYCHOTICS; EXPLANATORY "STUDY 008A" END 2021; START PHASE III Q1 2022, RESULTS Q3 2023; LAUNCH: 2025
PATHWAY	1) TWO POSITIVE PHASE III TRIALS (6 MONTHS TREATMENT); 2) AT LEAST 1,500 TREATED (INCL. SEVERAL HUNDRED 6 MONTHS); 3) AT LEAST 100 TREATED FOR 1 YEAR
PATIENT	POORLY RESPONDING PATIENTS CAN POTENTIALLY REGAIN A NORMAL SOCIAL AND PRODUCTIVE LIFE WITH A HIGHER LIFE EXPECTANCY
PHYSICIAN	POTENTIAL TO ADDRESS POORLY RESPONDING PATIENTS OR PATIENTS WITH BREAKTHROUGH SYMPTOMS ON CURRENT ANTIPSYCHOTIC TREATMENT
PAYER	SUBSTANTIAL REDUCTION OF ASSOCIATED COSTS SUCH AS UNEMPLOYMENT, LONG-TERM CARE, HOSPITALIZATION, SUICIDE RISK
PARTNER	PHASE IIA POC COMPLETED; NEXT STEPS: FUNDS SECURED TO START PHASE IIB/III REGISTRATIONAL TRIAL; GLOBAL PARTNERING ON PHASE IIB/III RESULTS

REVENUE MODEL

EUROPE / REST OF WORLD (PARTNER TBD)	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E
NUMBER OF PATIENTS (MN)	5.5	5.6	5.6	5.7	5.8	5.9	6.0	6.1	6.2	6.3	6.4
GROWTH (%)	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%
PERCENTAGE WITH POSITIVE SYMPTOMS (%)	70%	70%	70%	70%	70%	70%	70%	70%	70%	70%	70%
PATIENTS WITH POSITIVE SYMPTOMS (MN)	3.8	3.9	3.9	4.0	4.1	4.1	4.2	4.3	4.3	4.4	4.4
COMPLIANCE RATE (%)	25%	25%	25%	25%	25%	25%	25%	25%	25%	25%	25%
PATIENTS TREATED	958'249	972'623	987'212	1'002'020	1'017'051	1'032'306	1'047'791	1'063'508	1'079'460	1'095'652	1'112'087
-/- PATIENTS WITH CTRS	47'095	47'801	48'518	49'246	49'985	50'735	51'496	52'268	53'052	53'848	54'656
PATIENTS TREATED WITHOUT CTRS	911'154	924'821	938'694	952'774	967'066	981'572	996'295	1'011'240	1'026'408	1'041'804	1'057'432
PENETRATION (%)	0%	0%	0%	0%	0%	5%	8%	10%	11%	13%	15%
NUMBER OF TREATED PATIENTS	0	0	0	0	0	44'171	74'722	96'068	107'773	130'226	153'328
COST OF THERAPY PER YEAR (EUR)	3'650	3'650	3'650	3'650	3'650	3'650	3'650	3'650	3'650	3'650	3'650
SALES (EUR MN)	**0**	**0**	**0**	**0**	**0**	**161**	**273**	**351**	**393**	**475**	**560**
CHANGE (%)							69%	29%	12%	21%	18%
ROYALTY (%)	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%
ROYALTIES (EUR MN)	0	0	0	0	0	32	55	70	79	95	112
UPFRONT & MILESTONE PAYMENTS (EUR MN)			10	30	10			30			50
R&D COSTS	-4	-4	-10	-7	-4	0	0	0	0	0	0
PROFIT BEFORE TAX (EUR MN)	**-4**	**-4**	**0**	**23**	**6**	**32**	**55**	**100**	**79**	**95**	**162**
TAXES (EUR MN)	0	0	0	-4	-1	-10	-17	-31	-25	-30	-51
PROFIT (EUR MN)	**-4**	**-4**	**0**	**19**	**5**	**22**	**37**	**69**	**54**	**65**	**111**

UNITED STATES (PARTNER TBD)	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E
NUMBER OF PATIENTS (MN)	2.6	2.6	2.6	2.7	2.7	2.8	2.8	2.8	2.9	2.9	3.0
GROWTH (%)	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%
PERCENTAGE WITH POSITIVE SYMPTOMS (%)	70%	70%	70%	70%	70%	70%	70%	70%	70%	70%	70%
PATIENTS WITH POSITIVE SYMPTOMS (MN)	1.8	1.8	1.8	1.9	1.9	1.9	2.0	2.0	2.0	2.0	2.1
COMPLIANCE RATE (%)	25%	25%	25%	25%	25%	25%	25%	25%	25%	25%	25%
PATIENTS TREATED	446'808	453'510	460'313	467'218	474'226	481'339	488'559	495'888	503'326	510'876	518'539
-/- PATIENTS WITH CTRS	21'959	22'289	22'623	22'962	23'307	23'656	24'011	24'371	24'737	25'108	25'485
PATIENTS TREATED WITHOUT CTRS	424'849	431'222	437'690	444'255	450'919	457'683	464'548	471'516	478'589	485'768	493'055
PENETRATION (%)	0%	0%	0%	0%	1%	6%	10%	13%	15%	17%	18%
NUMBER OF TREATED PATIENTS	0	0	0	0	4'742	28'880	48'856	64'465	75'499	86'849	93'337
COST OF THERAPY PER YEAR (EUR)	4'793	4'593	4'593	4'593	4'593	4'593	4'593	4'593	4'593	4'593	4'593
SALES (EUR MN)	**0**	**0**	**0**	**0**	**22**	**133**	**224**	**296**	**347**	**399**	**429**
CHANGE (%)						509%	69%	32%	17%	15%	7%
ROYALTY (%)	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%
ROYALTIES (EUR MN)	0	0	0	0	4	27	45	59	69	80	86
UPFRONT & MILESTONE PAYMENTS (EUR MN)	0	0	8	25	8	0	0	25	0	0	34
PROFIT BEFORE TAX (USD MN)	**0**	**0**	**10**	**30**	**15**	**32**	**53**	**101**	**83**	**95**	**142**
TAXES (EUR MN)	0	0	0	-5	-2	-8	-14	-26	-22	-25	-37
PROFIT (EUR MN)	**0**	**0**	**8**	**20**	**11**	**18**	**31**	**58**	**48**	**55**	**82**

	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E
GLOBAL SALES (EUR MN)	**0**	**0**	**0**	**0**	**22**	**294**	**497**	**647**	**740**	**874**	**988**
CHANGE (%)						1249%	69%	30%	14%	18%	13%
GLOBAL PROFIT (EUR MN)	**-4**	**-4**	**8**	**39**	**16**	**40**	**68**	**127**	**102**	**120**	**193**
CHANGE (%)	33%	0%	-299%	391%	-60%	155%	69%	86%	-20%	18%	61%

WACC (%)	7%	
NPV TOTAL PROFIT (CHF MN)	**681**	
NUMBER OF SHARES (MN)	17.8	
NPV PER SHARE (CHF)	38	
SUCCESS PROBABILITY	15%	(PROOF-OF-CONCEPT ESTABLISHED)
RISK ADJUSTED NPV PER SHARE (CHF)	**5.7**	

SENSITIVITY ANALYSIS

		WACC (%)				
	CHF/SHARE	6.0	6.5	7.0	7.5	8.0
	65%	26.9	25.9	24.8	23.8	22.9
	55%	22.8	21.9	21.0	20.2	19.4
	45%	18.7	17.9	17.2	16.5	15.8
SUCCESS PROBABILITY	35%	14.5	13.9	13.4	12.8	12.3
	25%	10.4	9.9	9.5	9.2	8.8
	15%	6.2	6.0	**5.7**	5.5	5.3
	5%	2.1	2.0	1.9	1.8	1.8

ESTIMATES AS OF 5 MAY 2021

SOURCE: VALUATIONLAB ESTIMATES

Clozapine treatment-resistant schizophrenia (orphan-like indication)

EVENAMIDE - FINANCIAL FORECASTS FOR CLOZAPINE TREATMENT-RESISTANT SCHIZOPHRENIA (CTRS)

INDICATION	ADD-ON THERAPY TO ANTIPSYCHOTICS FOR REDUCING POSITIVE SYPMTOMS & PSYCHOTIC WORSENING IN CLOZAPINE TREATMENT-RESISTANT SCHIZOPHRENIA (CTRS)
DOSAGE	15-25 MG TWICE DAILY (TBD)
PRICE	USA: USD 15/DAY, EU/ROW: EUR 10/DAY; PRICING MAY PROVE CONSERVATIVE IF EVENAMIDE BECOMES A NEW TREATMENT PARADIGM IN SCHIZOPHRENIA
STANDARD OF CARE	CLOZAPINE AND OTHER ATYPICAL (2ND GENERATION) ANTIPSYCHOTICS SUCH AS ZYPREXA (OLANZAPINE), SEROQUEL (QUETIAPINE), RISPERDAL (RISPERIDONE)
UNIQUE SELLING POINT	POTENTIALLY FIRST ADD-ON THERAPY TO ANTIPSYCHOTICS IN PATIENTS WITH CLOZAPINE TREATMENT-RESISTANT SCHIZOPHRENIA (ORHPAN INDICATION)

7Ps ANALYSIS

PATENT	US: PATENT PROTECTION UNTIL 2033 BASED ON COMPOSITION OF MATTER PATENT GRANTED UNTIL 2028 + 5 YEARS EXTENSION; EU: 10-YEARS DATA EXCLUSIVITY
PHASE	FILINGS RELATING TO ORPHAN/PRIME/FAST TRACT DESIGNATION; START PHASE III Q1 2022, RESULTS Q3 2023; FILING Q4 2023; US LAUNCH MID 2024
PATHWAY	1) PHASE III TRIAL FOR ORPHAN INDICATION (CTRS); 2) PHASE III TRIAL FOR MAJOR INDICATION (SCHIZOPHRENIA); 18 MONTHS TO COMPLETION FOR BOTH TRIALS
PATIENT	CLOZAPINE TREATMENT-RESISTANT SCHIZOPHRENIA PATIENTS CAN POTENTIALLY REGAIN A NORMAL SOCIAL AND PRODUCTIVE LIFE WITH A HIGHER LIFE EXPECTANCY
PHYSICIAN	POTENTIAL TO ADDRESS TREATMENT-RESISTANT PATIENTS WHERE CLOZAPINE NO LONGER WORKS OR OTHER ATYPICAL ANTIPSYCHOTICS
PAYER	TREATMENT-RESISTANT SCHIZOPHRENIA IS ASSOCIATED WITH SOME OF THE HIGHEST HOSPITALIZATION COSTS, COSTS TO SOCIETY AND RISK OF SUICIDE
PARTNER	PHASE IIA POC COMPLETED IN SCHIZOPHRENIA; FUNDS SECURED TO COMPLETE BOTH PHASE III TRIALS; OWN US SALES FORCE, PARTNERING ON PHASE III IN EU/ROW

REVENUE MODEL

EUROPE / REST OF WORLD (PARTNER TBD)	**2020E**	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**
NUMBER OF PATIENTS (MN)	5.5	5.6	5.6	5.7	5.8	5.9	6.0	6.1	6.2	6.3	6.4
GROWTH (%)	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%
PERCENTAGE WITH POSITIVE SYMPTOMS (%)	70%	70%	70%	70%	70%	70%	70%	70%	70%	70%	70%
PATIENTS WITH POSITIVE SYMPTOMS (MN)	3.8	3.9	3.9	4.0	4.1	4.1	4.2	4.3	4.3	4.4	4.4
TREATMENT-RESISTANT SCHIZOPHRENIA (%)	35%	35%	35%	35%	35%	35%	35%	35%	35%	35%	35%
TREATMENT-RESISTANT SCHIZOPHRENIA PATIENTS	1'341'549	1'361'672	1'382'097	1'402'828	1'423'871	1'445'229	1'466'907	1'488'911	1'511'245	1'533'913	1'556'922
PATIENTS ON CLOZAPINE (%)	12%	12%	12%	12%	12%	12%	12%	12%	12%	12%	12%
PATIENTS ON CLOZAPINE	156'983	159'338	161'728	164'154	166'616	169'116	171'652	174'227	176'841	179'493	182'186
CLOZAPINE-RESISTANT SCHIZOPHRENIA (%)	30%	30%	30%	30%	30%	30%	30%	30%	30%	30%	30%
CLOZAPINE-RESISTANT SCHIZOPHRENIA PATIENTS	47'095	47'801	48'518	49'246	49'985	50'735	51'496	52'268	53'052	53'848	54'656
PENETRATION (%)	0%	0%	0%	0%	2%	12%	20%	26%	30%	32%	33%
NUMBER OF TREATED PATIENTS	0	0	0	0	1'000	6'088	10'299	13'590	15'916	17'231	18'036
COST OF THERAPY PER YEAR (EUR)	3'650	3'650	3'650	3'650	3'650	3'650	3'650	3'650	3'650	3'650	3'650
SALES (EUR MN)	**0**	**0**	**0**	**0**	**4**	**22**	**38**	**50**	**58**	**63**	**66**
CHANGE (%)						509%	69%	32%	17%	8%	5%
ROYALTY (%)	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%
ROYALTIES (EUR MN)	0	0	0	0	1	4	8	10	12	13	13
UPFRONT & MILESTONE PAYMENTS (EUR MN)			5	10	5			5			
R&D COSTS	-1	-1	-4	-3	0	0	0	0	0	0	0
PROFIT BEFORE TAX (EUR MN)	**-1**	**-1**	**1**	**7**	**6**	**4**	**8**	**15**	**12**	**13**	**13**
TAXES (EUR MN)	0	0	0	-1	-1	-1	-2	-5	-4	-4	-4
PROFIT (EUR MN)	**-1**	**-1**	**1**	**6**	**5**	**3**	**5**	**10**	**8**	**9**	**9**

UNITED STATES (NEWRON SPECIALIST SALES FORCE)	**2020E**	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**
NUMBER OF PATIENTS (MN)	2.6	2.6	2.6	2.7	2.7	2.8	2.8	2.8	2.9	2.9	3.0
GROWTH (%)	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%
PERCENTAGE WITH POSITIVE SYMPTOMS (%)	70%	70%	70%	70%	70%	70%	70%	70%	70%	70%	70%
PATIENTS WITH POSITIVE SYMPTOMS (MN)	1.8	1.8	1.8	1.9	1.9	1.9	2.0	2.0	2.0	2.0	2.1
TREATMENT-RESISTANT (%)	35%	35%	35%	35%	35%	35%	35%	35%	35%	35%	35%
TREATMENT-RESISTANT SCHIZOPHRENIA	625'532	634'914	644'438	654'105	663'916	673'875	683'983	694'243	704'657	715'226	725'955
PATIENTS ON CLOZAPINE (%)	12%	12%	12%	12%	12%	12%	12%	12%	12%	12%	12%
PATIENTS ON CLOZAPINE	73'197	74'295	75'410	76'541	77'689	78'854	80'037	81'238	82'456	83'693	84'949
CLOZAPINE-RESISTANT SCHIZOPHRENIA (%)	30%	30%	30%	30%	30%	30%	30%	30%	30%	30%	30%
CLOZAPINE-RESISTANT SCHIZOPRENIA PATIENTS	21'959	22'289	22'623	22'962	23'307	23'656	24'011	24'371	24'737	25'108	25'485
PENETRATION (%)	0%	0%	0%	0%	3%	18%	30%	40%	48%	49%	50%
NUMBER OF TREATED PATIENTS	0	0	0	0	699	4'258	7'203	9'749	11'874	12'303	12'615
COST OF THERAPY PER YEAR (EUR)	4'793	4'593	4'593	4'593	4'593	4'593	4'593	4'593	4'593	4'593	4'593
SALES (EUR MN) - BOOKED BY NEWRON	**0**	**0**	**0**	**0**	**3**	**20**	**33**	**45**	**55**	**57**	**58**
CHANGE (%)						509%	69%	35%	22%	4%	3%
COGS (%)	15%	15%	15%	15%	15%	15%	15%	15%	15%	15%	15%
COGS (EUR MN)	0	0	0	0	0	-3	-5	-7	-8	-8	-9
S,G&A (%)	0%	0%	0%	0%	261%	50%	30%	25%	20%	20%	20%
S,G&A (EUR MN)	0	0	0	0	-8	-10	-10	-11	-11	-11	-12
PROFIT BEFORE TAX (EUR MN)	**0**	**0**	**0**	**0**	**-6**	**7**	**18**	**27**	**35**	**37**	**38**
TAXES (EUR MN)	0	0	0	0	1	-2	-6	-8	-11	-12	-12
PROFIT (EUR MN)	**0**	**0**	**0**	**0**	**-5**	**5**	**12**	**18**	**24**	**25**	**26**

	2020E	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**
GLOBAL SALES (EUR MN)	**0**	**0**	**0**	**0**	**7**	**42**	**71**	**94**	**113**	**119**	**124**
CHANGE (%)						509%	69%	34%	19%	6%	4%
GLOBAL PROFIT (EUR MN)	**-1**	**-1**	**1**	**6**	**0**	**8**	**18**	**29**	**32**	**34**	**35**
CHANGE (%)	0%	0%	-195%	498%	-99%	12959%	128%	62%	13%	5%	3%

WACC (%)	7%	
NPV TOTAL PROFIT (CHF MN)	**151**	
NUMBER OF SHARES (MN)	17.8	
NPV PER SHARE (CHF)	8	
SUCCESS PROBABILITY	15%	(PROOF-OF-CONCEPT ESTABLISHED)
RISK ADJUSTED NPV PER SHARE (CHF)	**1.3**	

SENSITIVITY ANALYSIS

		WACC (%)				
	CHF/SHARE	6.0	6.5	7.0	7.5	8.0
	65%	6.0	5.8	5.5	5.3	5.1
	55%	5.1	4.9	4.7	4.5	4.3
	45%	4.2	4.0	3.8	3.7	3.5
SUCCESS PROBABILITY	35%	3.2	3.1	3.0	2.9	2.7
	25%	2.3	2.2	2.1	2.0	2.0
	15%	1.4	1.3	**1.3**	1.2	1.2
	5%	0.5	0.4	0.4	0.4	0.4

ESTIMATES AS OF 5 MAY 2021

SOURCE: VALUATIONLAB ESTIMATES

Unique Selling Point

Evenamide will be uniquely developed as an add-on to mainstay antipsychotic therapy for schizophrenia patients who no longer adequately respond to their current therapy, including patients with clozapine treatment-resistant schizophrenia. Evenamide has the potential to prolong response rates of current antipsychotics and reduce the frequent switching of therapy in schizophrenia improve prescribing quality by providing an alternative to the practice of high-dose antipsychotic use that can be associated with higher adverse events and poor patient compliance.

7P's Analysis

Patent: Evenamide has a granted solid composition of matter patent with protection running until at least 2028. With 5 years patent extension terms, protection runs until 2033. Evenamide will enjoy at least 10 years data protection from approval in the EU. Fixed-dose combinations with current antipsychotics could markedly extend evenamide's patent life.

Phase: Newron has successfully completed a phase IIa POC trial in schizophrenia, which justifies a 15% success probability. The start of the two potentially pivotal trials in schizophrenia and CTRS in Q1 2022 justifies a 50% (potentially pivotal phase II/III trials) success rate with our rNPV jumping by a staggering CHF 16.4 per share. Topline results in schizophrenia and CTRS are expected in Q3 2023.

Pathway: To gain approval in the US and EU, Newron will have to submit two pivotal phase III trials as an add-on to other antipsychotics; grant of a breakthrough designation for CTRS may reduce this to one cross-supportive trial for each indication. Usually, at least 1,500 patients treated with evenamide, including several hundred treated 6 months, and at least 100 treated 1 year are required.

Patient: Adding evenamide to a patient's current therapy once the patient no longer adequately responds provides a more stable treatment regimen than e.g. switching to another antipsychotic with a different dosing regime, effect and side effects. Evenamide has the potential to prolong the patient's response to effective antipsychotics and restore normal social and economic life.

Physician: The physician can maintain patients on antipsychotic therapy where they initially responded but where the effect wanes over time. By simply adding evenamide therapy response is restored and prolonged without the need to switch a patient to another antipsychotic treatment with a different risk benefit profile.

Payer: Prolonging the effect of mainstay antipsychotic treatment avoids the cost of switching to other treatments with the potential to reduce other costs such as inpatient and outpatient and long-term care, and costs that arise from the productivity loss suffered by individuals with schizophrenia.

Partner: Upon positive "Study 008A" results by end 2021, we assume Newron will sign on a major CNS commercialization partner for schizophrenia globally and CTRS outside the US. We assume upfront, development and sales milestones of up to EUR 298 mn with 20% royalties on sales. We assume Newron will commercialize evenamide in CTRS in the US through an own small specialist sales force. Currently, Newron is evaluating potential options for partnering or co-developing evenamide.

Schizophrenia Disease Market

The market for antipsychotics was valued at USD 12 bn in 2015, of which approximately half were for treating schizophrenia, according to Grand View Research. Over the last few years the market has been shrinking due to patent expirations of key brands such as Eli Lilly's Zyprexa, AstraZeneca's Seroquel, Pfizer's Geodon and Otsuka/Bristol-Myer Squibb's Abilify. The market is expected to bounce back thanks to new (long-acting) formulations of existing drugs that command higher prices and new drugs that can be priced at a premium. For instance, JNJ's Invega Trinza, a long-acting injectable version of Risperdal, generated sales of USD 641 mn in 2016. New formulation sales are expected amount to USD 3 bn 2021 with the total schizophrenia market amounting to almost USD 8 mn. Population growth will also help push up the number of patients who need treatment.

SCHIZOPHRENIA - KEY FACTS	
MARKET SIZE	USD ~6 BN
PREVALENCE	>21 MN GLOBALLY, ~2.4 MN IN US, ~5.2 MN IN EU/ROW (JAP/AUS/CAN)
INCIDENCE	~1.5 MN GLOBALLY; ~100,000 IN US, ~220,000 IN EU/ROW (JAP/AUS/CAN)
UNDERLYING CAUSE	LARGELY UNKNOWN, COMPLEX INTERPLAY OF GENETICS, BRAIN CHEMISTRY AND STRUCTURE (NEUROTRANSMITTERS), PROBLEMS DURING PREGNANCY, AND ENVIRONMENT; USUALLY STARTS IN LATE ADOLESCENCE OR EARLY ADULTHOOD AND IS A LIFELONG CONDITION
SYMPTOMS	- "POSITIVE" SYMPTOMS, INCLUDING: - DELUSIONS (OF REFERENCE, PARANOID, SOMATIC, GRANDEUR) - HALLUCINATIONS (VISUAL, AUDITORY, TACTILE, OLFACTORY, GUSTATORY) - DISORGANIZED SPEECH - GROSSLY DISORGANIZED OR CATATONIC BEHAVIOUR - "NEGATIVE SYMPTOMS" INCLUDING: - LACK OF EMOTION/INTEREST - LOW ENERGY - AFFECTIVE FLATTENING - SOCIAL ISOLATION
DRUG CLASS (KEY BRANDS)	- TRADITIONAL, 1ST GEN. ANTIPSYCHOTICS: (HALDOL, THORAZINE, STELAZINE) - ATYPICAL, 2ND GEN. ANTIPSYCHOTICS: (CLOZARIL, GEODON, SEROQUEL, RISPERDAL, ZYPREXA, SYMBYAX, ABILIFY, INVEGA, SAPHIRIS)
MAJOR PLAYERS (KEY BRANDS)	- ELI LILLY (ZYPREXA, SYMBYAX) - JOHNSON & JOHNSON (RISPERDAL, INVEGA) - ASTRAZENECA (SEROQUEL) - PFIZER (GEODON) - BRISTOL-MYERS SQUIBB (ABILIFY) - NOVARTIS (CLOZARIL) - MERCK & CO (SAPHIRIS) - DAINIPPON SUMITOMO PHARMA (LONASEN)

ESTIMATES AS OF APRIL 19, 2017 SOURCE: VALUATIONLAB, NIH, WHO, COMPANY REPORTS

According to the WHO, there are more than 21 mn people suffering from either schizophrenia or similar symptoms. Schizophrenia is a chronic and severe mental disorder that affects how a person thinks, feels, and behaves. People with schizophrenia may seem like they have lost touch with reality. The underlying cause is unknown but is believed to be a complex interplay of genetics, brain structure and chemistry (e.g. imbalance of neurotransmitters such as dopamine and glutamate that brain cells use to communicate with each other), developmental (e.g. hypoxia or infection during fetal development) and environmental factors, such as excessive substance use. Although schizophrenia is not as common as other mental disorders, the symptoms can be very disabling.

Symptoms of schizophrenia usually start between ages 16 and 30. The symptoms of schizophrenia fall into three categories:

1. **Positive symptoms:** these symptoms are psychotic behaviors not generally seen in healthy people. People with positive symptoms may lose touch with some aspects of reality, and include hallucinations, delusions, thought disorders (unusual or dysfunctional ways of thinking), movement disorders (agitated body movements)
2. **Negative symptoms:** these symptoms are associated with disruptions to normal

emotions and behaviors. Symptoms include flat affect (reduced expression of emotions via facial expression or voice tone), reduced feelings of pleasure in everyday life, difficulty beginning and sustaining activities, reduced speaking

3. **Cognitive symptoms:** for some patients, the cognitive symptoms of schizophrenia are subtle, but for others, they are more severe, and patients may notice changes in their memory or other aspects of thinking. Symptoms include poor executive functioning (the ability to understand information and use it to make decisions), trouble focusing or paying attention, problems with working memory (the ability to use information immediately after learning it)

Current drug treatment falls short in treating symptoms with low patient compliance
Because the causes of schizophrenia are still unknown, treatments focus on eliminating the symptoms of the disease. Antipsychotic medications are the cornerstone for the treatment of schizophrenia, often in combination with psychological and social supports. Antipsychotic drugs help to normalize the biochemical balances that cause schizophrenia.
There are two major types of antipsychotics:

1. **First-generation (typical) antipsychotics:** such as Haldol (haloperidol), Thorazine (chlorpromazine), Stelazine (trifluoperazine), primarily block dopamine receptors and were the first drugs approved for treating schizophrenia more than 50 years ago. Although they were effective in treating positive symptoms, they were associated with a high occurrence of extrapyramidal side effects (EPS). This led to the development of second-generation (atypical) antipsychotics, which did not carry the risk of EPS and demonstrated a greater clinical benefit in patients.
2. **Second-generation (atypical) antipsychotics:** such as Novartis' Clozaril (clozapine), JNJ's Risperdal (risperidone), Eli Lilly's Zyprexa (olanzapine), AstraZeneca's Seroquel (quetiapine), Pfizer's Geodon (ziprasidone hydrochloride), Lundbeck's Abilify (aripiprazole), and JNJ's Invega (paliperidone) work on both the serotonin and dopamine receptors and have been available since the 1990's. These drugs appear to be more effective in treating a broader range of symptoms of schizophrenia, however, are associated with considerable weight gain, diabetes and risk of metabolic syndrome, most pronounced with Zyprexa.

Current approved medications for schizophrenia address positive symptoms but fall short in treating negative and cognitive symptoms. It is estimated that 75% of all patients stop taking their medications, regardless of which generation, because they did not make the better or had intolerable side effects. Discontinuation rates remain high even when patients are switched to a new drug, which is often the case

New market entrants
New market entrants include new formulations of existing drugs or combinations of drugs that enhance patient compliance (e.g. controlled release, depot formulations). New approaches to treat schizophrenia - some potentially addressing negative and cognitive symptoms - include, AMPA receptor modulators (Biogen's **BIIB-104** – phase II), sodium channel blockers (Newron's evenamide – POC completed), 5-HT2A receptor antagonists (Intra-Cellular Therapies' **Caplyta** (lumateperone) FDA approved in 2019, Minerva Neurosciences' **roluperidone** – phase III), 5-HT6 receptor antagonists (Avineuro's **avisetron** – phase II/III), and the positive allosteric modulator of the alpha7 nicotinic acetylcholine receptor (**AVL-3288** – phase I), among others.

Xadago (Parkinson's disease)

Product Analysis

Xadago all indications: Peak sales EUR 400+ mn; Risk-adjusted NPV CHF 5.8/share

1) Parkinson's peak sales of EUR 200+ mn - rNPV of CHF 5.4 per share

We forecast peak sales of EUR 227 mn for Xadago in its major indication Parkinson's disease. Xadago was launched in the EU in 2015 followed by the US in 2017, and in Japan in 2019. We assume global patent protection until 2029 (including 5 years patent term extensions), a daily treatment cost of USD 9 (US), EUR 2.80 (EU/ROW) and EUR 4 (Japan/Asia), and a market penetration peaking between ~4-5%, hampered by cheap generic versions of Teva's Azilect (rasagiline). Our NPV amounts to CHF 97 mn, or CHF 5.4 per share, assuming Newron receives EUR 10 mn remaining milestone payments, royalties on sales ranging between 2.5% (Japan), 7.5% (US) and 10-15% (EU/ROW), with a WACC of 7% reflecting the low Swiss interest environment (for details see page 39).

2) PD-LID peak sales of EUR 200 mn – rNPV of CHF 0.4 per share

For Xadago's planned line extension in PD-LID (Parkinson's disease levodopa-induced dyskinesia), defined by the FDA as an orphan indication, to strengthen its label, we forecast peak sales of EUR 206 mn. The single potentially pivotal trial is planned to start in Q1 2022 with first approvals expected in 2024. We assume similar dosing and pricing for Xadago in PD-LID as in Parkinson's disease and a market penetration conservatively peaking between ~5-6%. Our rNPV amounts to CHF 7 mn or CHF 0.4 per share with a conservative 15% (proof-of-concept) success probability (for details see page 40).

PD-LID – new orphan indication label to boost sluggish sales

Xadago is Newron's first ever launched product stemming from its own ion channel research and was launched in the EU in 2015, in the US in 2017 and in Japan in 2019 for treating mid to late stage Parkinson's patients experiencing "off" episodes in combination with mainstay levodopa or other Parkinson medications (~80% of treated patients). Xadago is the first NCE (new chemical entity) approved in over a decade for treating Parkinson's disease.

In 2012, Xadago was licensed to Meiji Seika (Japan & Asian markets) and Zambon (worldwide excluding Meiji Seika markets). Xadago is commercialized by these partners and their sublicensees (e.g. Supernus Pharma in the US, Medison Parma for Israel), while Newron receives milestone and (low) royalty payments from sales of Xadago. Xadago has now been launched in more than 15 European countries with more countries to follow.

In 2017, partner Zambon entered into a partnership with Seqirus for commercialization of Xadago in Australia (approved in November 2018) and New Zealand and with Valeo for Canada (branded "Onstryv" and launched in July 2019), while Eisai acquired exclusive rights of Xadago for Japan and Asia from Newron's Japanese development partner Meiji Seika. In September 2019, the drug was approved in Japan and branded "Equfina"

Zambon and its regional partners have gained approval for Xadago further in Brazil, Colombia and Israel with launches expected to occur in the next 12 months, while dossiers for marketing authorization are currently under review in Mexico. Furthermore, Zambon is

in discussions for additional Xadago distribution agreements in Southern Europe, the Middle East, Africa and South America.

PD-LID label extension to enhance sales uptake and underline unique offering

Xadago product sales have trailed expectations due to a slower uptake, in particular in the US, by US WorldMeds due to difficult market conditions where cheap generic versions of Teva's Azilect (rasagiline) have become available. Supernus Pharma will now be responsible for US commercialization of Xadago after the company acquired US WorldMeds' CNS portfolio in June 2020, which may provide a much-needed sales spur.

In March 2021, Newron and partner Zambon signed an agreement to start a potentially pivotal trial to evaluate the efficacy of Xadago in Parkinson disease patients with levodopa-induced dyskinesia (PD-LID), an important label extension and differentiation for Xadago in key markets. PD-LID is a debilitating side effect of long-term use with mainstay Parkinson's treatment levodopa and is considered an orphan disease with less than 200,000 patients in the US. Newron and Zambon will share the costs of the trial equally, and in return, Newron will qualify for a one-time milestone payment and a greater share of royalties should the trial lead to a label extension. Currently, the only treatment specifically approved for PD-LID is Adamas' Gocovri, an extended-release formulation of generic amantadine, with an annual treatment price of approximately USD 26,000 per patient, which was launched in the US in October 2017. Gocovri sales amounted to USD 71 mn in 2020, despite warnings and precautions including, falling asleep during activities of daily living, suicidality and depression, and hallucinations and psychotic behavior, among others.

Xadago reduced dyskinesia by about 39% in registrational trial for Parkinson's

In Xadago's pivotal phase III trials, which led to approval in Parkinson's disease, the compound showed a long-lasting (2-years) effect on reducing dyskinesia in the double-blind placebo-controlled extension trial "Study 016/018" in patients experiencing dyskinesia at baseline by about 37%. The double-blind, placebo-controlled trial will be conducted in the US, Europe and Asia/Australia, with the aim of an important label extension and differentiation for Xadago in key markets. As PD-LID is considered an orphan indication in the US, this allows for faster review times. The PD-LID trial is expected to start in Q1 2022 with topline results expected two years later.

Xadago can piggyback on the commercial success of Azilect without competition

Xadago is a so-called MAO-B inhibitor and belongs to the same class as Teva's Azilect (rasagiline). We believe Xadago has the potential to piggyback on the commercial success of Azilect, with a similar positioning in patients with mid to late stage disease. Importantly, Xadago has several advantages, in particular with regards to safety and tolerability and long-term efficacy. The positioning of Xadago by Supernus Pharma will be critical. Azilect no longer enjoys patent protection in the US since February 2017, with cheap generics now replacing the branded product. Global sales of Azilect peaked at USD 700 mn in 2014, the year before it lost patent protection in several EU countries, with the bulk of sales stemming from patients with mid to late stage disease.

Xadago could be positioned as the new cornerstone therapy next to levodopa for patients with mid to late stage disease. Xadago is the first new chemical entity approved for Parkinson's disease for over a decade with many physicians eager to find out how the drug can help treat patients who no longer adequately respond to mainstay levodopa treatment or are affected by treatment side effects. These side effects typically develop after 4–10

years of levodopa therapy and affect approximately 50-75% of all patients. The "wearing-off" effect is the most common type, and “delayed-on,” “no-on,” and “on-off” fluctuations, as well as dyskinesia and cognitive worsening, may also develop as the disease progresses.

Treatment goal is to limit or delay the onset of levodopa-related complications
Collectively, motor fluctuations represent a significant source of disability in advanced Parkinson's patients, and reducing these is a major goal of patient management. Adjunctive medications, including dopamine agonists, anticholinergics, MAO-B inhibitors, and COMT inhibitors, each may reduce the frequency or duration of “off” periods, but none does so completely, and each contributes its own side effects which may limit optimal dosing. These problems have led to the development of strategies, which aim to limit or delay the onset of levodopa-related complications and have become the key drivers for the Parkinson's disease market. We believe Xadago with its unique dual mechanism of action and excellent tolerability profile is well positioned.

Xadago is a MAO-B inhibitor with unique and attractive qualities
Although Azilect and Xadago both belong to the MAO-B inhibitor class, we believe Xadago has distinct properties, which can position the compound as the new cornerstone therapy in treating patients with mid to late stage Parkinson’s disease.

Xadago is believed to be a unique compound with a novel **dual mechanism** of action based on:

1) **The enhancement of the dopaminergic function** (through potent reversible inhibition of MAO-B and of dopamine uptake)
2) **Ion channel blockade** that leads to inhibition of stimulated release of glutamate (which may be the mechanism underlying potential neuro-protecting and anti-dyskinetic properties).

There are no head-to-head clinical studies of Azilect and Xadago, making comparisons difficult. However, certain observations can be made.

- Xadago is a reversible MAO-B inhibitor, whereas Azilect is an irreversible MAO-B inhibitor given its long half-life. This can be an important safety aspect in case of serious side effects caused by e.g. drug interactions; Xadago is cleared faster out of the body. Xadago appears to have a superior side effect profile in patients with mid to late stage Parkinson’s disease who are treated with levodopa and other medications.
- Xadago has unparalleled 18/24 months clinical data backing long-term efficacy and safety
- Xadago improves “on-time” without troublesome dyskinesia – this is the quality time patients are seeking; reducing “off-time”, Azilect’s primary endpoint, does not translate directly in improving “on-time” without troublesome dyskinesia
- Xadago has a fast onset of action, which lasts up to 2 years (backed by double-blinded clinical trials)
- Xadago has the potential to reduce (levodopa-induced) dyskinesia due to its unique ability to reduce glutamatergic activity (needs to be further investigated)
- Xadago has the potential to reduce depression due to its unique ability to reduce glutamatergic activity (needs to be further investigated)

Superior safety and tolerability when compared to Azilect

The difference in safety and tolerability is apparent when we compare Xadago and Azilect based on the US prescribing information or so-called label provided by the FDA. The label is the key marketing message a company may actively promote to physicians.

ADVERSE EVENTS COMPARISON

ADVERSE EVENTS > 2%	AZILECT "STUDY 3" (+ L-DOPA); 26 WEEKS			XADAGO "STUDIES 1 & 2" (+ L-DOPA); 24 WEEKS		
	1 MG/DAY (N=149)	0.5 MG/DAY (N=164)	PLACEBO (N=159)	50 MG/DAY (N=223)	100 MG/DAY (N=498)	PLACEBO (N=497)
	(%)	(%)	(%)	(%)	(%)	(%)
DYSKINESIA (UNCONTROLLABLE MOVEMENT)	**18**	**18**	10	**21**	**17**	9
FALL	**11**	**12**	8	4	6	4
NAUSEA (DISCOMFORT UPPER STOMACH)	**12**	10	8	3	6	4
INSOMNIA (SLEEPLESSNESS)				1	4	2
ORTHOSTATIC HYPOTENSION (FALL IN BLOOD PRESSURE)	**9**	6	3	2	2	1
ANXIETY				2	2	1
COUGH				2	2	1
DYSPEPSIA (INDIGESTION)	5	4	4	0	2	1
ACCIDENTAL INJURY	**12**	8	5			
VOMITING	**7**	4	1			
CONSTIPATION	**9**	6	4			
ARTHRALGIA (JOINT PAIN)	**8**	6	4			
ABDOMINAL PAIN	**5**	2	1			
ANOREXIA (EATING DISORDER)	**5**	2	1			
HEADACHE	11	8	10			
WEIGHT LOSS	9	2	8			
ECCHYMOSIS (BRUISING)	5	2	3			
PARESTHESIA (PINS AND NEEDLES)	5	2	3			
SOMNOLENCE (SLEEPINESS)	6	4	4			
DRY MOUTH	6	2	3			
RASH	6	3	3			
DIARRHEA	5	7	4			
ABNORMAL DREAMS	4	1	1			
HALLUCINATIONS	4	5	3			
ATAXIA (UNCOORDINATED MUSCLE MOVEMENT)	3	6	1			
DYSPNEA (SHORTNESS OF BREATH)	3	5	2			
INFECTION	3	2	2			
SWEATING	3	2	1			
TENOSYNOVITIS (INFLAMMATION OF TENDON)	3	1	0			
DYSTONIA (MUSCLE CONTRACTIONS)	3	2	1			
GINGIVITIS (INFLAMMATION OF GUM TISSUE)	2	1	1			
HEMORRHAGE (BLEEDING)	2	1	1			
HERNIA	2	1	1			
MYASTHENIA (MUSCLE WEAKNESS)	2	2	1			

SOURCE: VALUATIONLAB, FDA PRESCRIBING INFORMATION

In the table above, we compared the adverse events, which occurred in more than 2% of treated patients for Azilect and Xadago in similar patient populations, namely in Parkinson's patients with mid to late stage disease patients treated with mainstay levodopa and other treatments such as dopamine agonists. As can be seen above, it is clear that Xadago has far less adverse events that occur in more than 2% of patients compared to Azilect. The most frequent adverse event that occurs with Xadago is dyskinesia, which occurs in a similar rate as with Azilect and is mostly transient in nature when therapy is started. With regards to all other frequent adverse events that occur with Azilect, the occurrence with Xadago is far less (e.g. fall, nausea, orthostatic hypotension) or less than 2% (e.g. accidental injury, vomiting, constipation, joint pain, abdominal pain, anorexia). Moreover, the incidence of hallucinations, dystonia (painful muscle contractions) and abnormal dreams, a main reason for patients to stop Azilect treatment, is below the 2% threshold with Xadago.

Xadago has the potential to reduce PD-LID over a long treatment period

Therefore, we believe Xadago has the potential to surpass Azilect as the leading MAO-B inhibitor in treating Parkinson's patients with mid to late stage disease thanks to its superior safety and tolerability profile and proven long-term efficacy up to 2 years of treatment. Moreover, Xadago has the potential to reduce dyskinesia in Parkinson's patients with moderate dyskinesia (DRS>4) as seen in "Study 016/018. Currently there are no drugs on the market that have shown reducing dyskinesia over such a period.

"Study 016/018" shows benefits maintained for at least 2 years

This double blind, placebo-controlled extension study, which was presented in 2011, shows the benefit of adding 50 or 100 mg/day of Xadago (safinamide) to levodopa in mid to late stage Parkinson's patients are maintained for at least 2 years. Several patient and physician-rated outcomes reached statistical significance including, total ON time, OFF time, PDQ total, UPDRS II, III & IV total.

"STUDY 016/018"	PLACEBO (N=69)	SAFINAMIDE 50 MG/DAY (N=78)	SAFINAMIDE 100 MG/DAY (N=74)
DYSKINESIA RATING SCALE			
- VALUE AT MONTH 24	7.0 +/- 3.53	6.6 +/- 3.54	6.4 +/- 4.45
- LS DIFFERENCE VS. PLACEBO	0.0	**-0.7**	**-1.22**
- P-VALUE VS. PLACEBO	N/A	0.1999	0.0317

SOURCE: NEWRON PHARMACEUTICALS

Importantly, in Parkinson's patients with moderate dyskinesia (DRS>4) at baseline "Study 016/018" showed under double-blind, placebo-controlled conditions that Xadago (safinamide) 100 mg/day reduces dyskinesia.

Global PD-LID trial expected to start in Q1 2022 (delayed by Covid-19 pandemic)

Based on the above findings, Newron and its partner Zambon, together with academic and regulatory experts, have designed a potentially pivotal efficacy study to evaluate the effects of Xadago in patients with levodopa-induced dyskinesia (PD-LID). The single, potentially pivotal efficacy trial with participating centers in the US, Europe and Asia/Australia enrolling more than 200 patients with a 2-years treatment duration is expected to start in Q1 2022.

Xadago has global peak sales potential of EUR 400+ mn

To correctly reflect and value Newron's plans to expand Xadago's label, we have made separate forecasts for PD-LID next to our current Parkinson's disease forecasts for Xadago (which we have conservatively lowered on the disappointing uptake in the US). Based on current pricing, we forecast global peak sales for Xadago of EUR 200 mn in PD-LID as well as EUR 200+ mn global peak sales in mid to late-stage Parkinson's disease. Xadago would provide a unique offering with a proven long-lasting effect on treating mid to late stage Parkinson's disease as an add-on to existing mainstay levodopa, while also reducing dyskinesia, the debilitating side effect of long-term levodopa use, at a far more attractive price than Gocovri.

1) Parkinson's disease (major indication) peak sales of EUR 200+ mn

We have used the same base for our forecasts for Xadago in mid to late stage Parkinson's disease as previously. However, we have excluded patients with PD-LID as these are now captured in our new forecasts for Xadago in PD-LID. In our detailed Xadago forecasts we have accounted for Newron's three major commercialization regions, namely:

1) **Europe/ROW (Zambon & partners):** we forecast peak sales to amount to EUR 123 mn assuming a daily treatment price of EUR 2.80 and a peak penetration rate of ~5%. We assume a tiered royalty rate from 10% to 14%.
2) **US (Supernus Pharma):** peak sales could amount to around EUR 105 mn with a daily treatment price of USD 9 and a peak penetration of ~4%. We assume further sales milestones of EUR 10 mn and royalties on sales of ~7.5% in the US.
3) **Japan/Asia (Meiji Seika & Eisai):** we forecast peak sales amounting to EUR 13 mn and royalties on sales to amount to ~2.5%.

2) PD-LID (orphan indication) peak sales of EUR 200 mn

We have based our Xadago forecasts for PD-LID on the number of patients with mid to late stage Parkinson's disease treated with levodopa that develop PD-LID after long-term use of this cornerstone treatment. We assume the same pricing for Xadago in PD-LID as for Parkinson's disease, which may prove to be conservative once the label is extended to treat PD-LID providing a unique treatment offering. Our peak sales forecast in Newron's three major commercialization regions amount to:

1) **Europe/ROW (Zambon & partners):** we forecast first launches to occur in 2024 with peak sales to amount to EUR 91 mn assuming a daily treatment price of EUR 2.80 and a conservative peak penetration rate of ~5%. We assume a royalty rate of ~14% with a one-time single digit million milestone payment.
2) **US (Supernus Pharma):** we forecast a 2024 launch and peak sales to amount to around EUR 108 mn with a daily treatment price of USD 9 and a conservative peak penetration of ~6%. We assume a ~8% royalty rate on sales with no additional milestone payments.
3) **Japan/Asia (Meiji Seika & Eisai):** we forecast a launch in 2025 with peak sales amounting to EUR 9 mn. We assume royalties on sales to amount to ~2.5% with no further milestone payments.

Our detailed forecasts and sensitivity analysis for Parkinson's disease and PD-LID can be seen on the following two pages.

Forecasts & Sensitivity Analysis

XADAGO (SAFINAMIDE) - FINANCIAL FORECASTS FOR PARKINSON'S DISEASE

INDICATION	ADD ON THERAPY TO LEVODOPA/CARBIDOPA OR IN COMBINATION WITH OTHER PARKINSON'S DISEASE (PD) DRUGS IN MID-TO-LATE STAGE PATIENTS
DOSAGE	50 OR 100 MG / DAY
PRICE	EUROPE/ROW: EUR 2.80 PER DAY; US: USD 10 PER DAY; JAPAN: EUR 4 PER DAY
STANDARD OF CARE	DOPAMINE AGONISTS (EARLY STAGE PD), LEVODOPA +/- CARBIDOPA (MID-TO-LATE STAGE PD)
UNIQUE SELLING POINT	1X DAILY ADD-ON THERAPY FOR MID-TO-LATE STAGE PARKINSON'S DISEASE WITH A UNIQUE DUAL MECHANISM OF ACTION WITH POTENTIAL ANTI-DYSKINETIC PROPERTIES

7Ps ANALYSIS

PATENT	PROTECTION EU (2029), US (2031): LEVODOPA COMBO PATENT 2026 (US) / 2024 (EU) + UP TO 5 YEAR EXTENSION I SYNTHESIS PATENT: 2027 I ANDA FILING REPORTED MAY 2021
PHASE	EU: APPROVED FEB 2015; US: APPROVED MAR 2017 (LAUNCH JULY 2017); JAPAN: APPROVED SEP 2019
PATHWAY	1) AT LEAST ONE POSITIVE PHASE III TRIAL (6 MONTHS TREATMENT), 2) AT LEAST 100 PATIENTS TREATED FOR 1 YEAR, 3) A TOTAL OF AT LEAST 1,500 TREATED PATIENTS
PATIENT	IMPROVING QUALITY OF LIFE IN EARLY DISEASE AND DELAYING IRREVERSIBLE SIDE EFFECTS SUCH AS DYSKINESIA RELATED TO LONG-TERM LEVODOPA USE
PHYSICIAN	HELPS DELAY USE OF MAINSTAY LEVODOPA TREATMENT THAT LEADS TO IRREVERSIBLE SIDE EFFECTS SUCH AS DYSKINESIA AND "WEARING OFF"
PAYER	DELAYS SIGNIFICANT COSTS RELATED TO DYSKINESIA AND "WEARING OFF" WHERE PATIENTS NEED EXTENSIVE CARE OR HAVE TO BE INSTITUTIONALIZED
PARTNER	ZAMBON (WORLDWIDE EXCL. JAPAN & KEY ASIAN MARKETS), MEIJI SEIKA (JAPAN & KEY ASIAN MARKETS) - NEWRON SHARES IN MILESTONE & ROYALTY PAYMENTS

REVENUE MODEL

EUROPE / REST OF WORLD (ZAMBON & PARTNERS)	**2020E**	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**
NUMBER OF PATIENTS (MN)	3.8	3.9	3.9	4.0	4.1	4.2	4.3	4.3	4.4	4.5	4.6
GROWTH (%)	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%
PATIENTS ON MEDICATION (%)	70%	70%	70%	70%	70%	70%	70%	70%	70%	70%	70%
PATIENTS TREATED	2,645,218	2,698,122	2,752,085	2,807,126	2,863,269	2,920,534	2,978,945	3,038,524	3,099,294	3,161,280	3,224,506
-/- PATIENTS WITH PD-LID	507,882	518,039	528,400	538,968	549,748	560,743	571,957	583,397	595,065	606,966	619,105
PATIENTS TREATED WITHOUT PD-LID	2,137,336	2,180,083	2,223,684	2,268,158	2,313,521	2,359,792	2,406,988	2,455,127	2,504,230	2,554,314	2,605,401
PENETRATION (%)	2.0%	2.1%	2.3%	2.8%	3.4%	3.9%	4.3%	4.6%	4.8%	3.4%	1.7%
NUMBER OF TREATED PATIENTS	41,926	46,035	51,403	63,772	78,928	92,306	103,780	113,221	120,494	86,032	43,877
COST OF THERAPY PER YEAR (EUR)	1,022	1,022	1,022	1,022	1,022	1,022	1,022	1,022	1,022	1,022	1,022
SALES (EUR MN)	**43**	**47**	**53**	**65**	**81**	**94**	**106**	**116**	**123**	**88**	**45**
CHANGE (%)	3%	10%	12%	24%	24%	17%	12%	9%	6%	-29%	-49%
ROYALTY (%)	10%	12%	12%	12%	14%	14%	14%	14%	14%	14%	14%
ROYALTIES (EUR MN)	4	6	6	8	11	13	15	16	17	12	6
UPFRONT & MILESTONE PAYMENTS (EUR MN)											
PROFIT BEFORE TAX (EUR MN)	**4**	**6**	**6**	**8**	**11**	**13**	**15**	**16**	**17**	**12**	**6**
TAXES (EUR MN)	0	0	0	-1	-2	-4	-5	-5	-5	-4	-2
PROFIT (EUR MN)	**4**	**6**	**6**	**6**	**10**	**9**	**10**	**11**	**12**	**8**	**4**

UNITED STATES (ZAMBON PARTNER SUPERNUS PHARMA)	**2020E**	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**
NUMBER OF PATIENTS (MN)	1.2	1.2	1.3	1.3	1.3	1.3	1.4	1.4	1.4	1.5	1.5
GROWTH (%)	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%
PATIENTS ON MEDICATION (%)	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%
PATIENTS TREATED	975,196	994,699	1,014,593	1,034,885	1,055,583	1,076,695	1,098,229	1,120,193	1,142,597	1,165,449	1,188,758
-/- PATIENTS WITH PD-LID	187,238	190,982	194,802	198,698	202,672	206,725	210,860	215,077	219,379	223,766	228,242
PATIENTS TREATED WITHOUT PD-LID	787,958	803,717	819,791	836,187	852,911	869,969	887,369	905,116	923,218	941,683	960,516
PENETRATION (%)	0.5%	0.7%	0.9%	1.2%	2.2%	2.8%	3.2%	3.4%	3.6%	3.8%	4.0%
NUMBER OF TREATED PATIENTS	4,078	5,767	7,522	9,762	18,487	24,076	28,107	30,480	32,936	35,478	38,108
COST OF THERAPY PER YEAR (EUR)	2,876	2,756	2,756	2,756	2,756	2,756	2,756	2,756	2,756	2,756	2,756
SALES (EUR MN)	**12**	**16**	**21**	**27**	**51**	**66**	**77**	**84**	**91**	**98**	**105**
CHANGE (%)	45%	36%	30%	30%	89%	30%	17%	8%	8%	8%	7%
ROYALTY (%)	7.5%	7.5%	7.5%	7.5%	8.0%	8.0%	8.0%	8.0%	8.0%	8.0%	8.0%
ROYALTIES (EUR MN)	1	1	2	2	4	5	6	7	7	8	8
UPFRONT & MILESTONE PAYMENTS (EUR MN)											
PROFIT BEFORE TAX (EUR MN)	**1**	**1**	**2**	**2**	**4**	**5**	**6**	**17**	**7**	**8**	**13**
TAXES (EUR MN)	0	0	0	0	-1	-2	-2	-5	-2	-2	-4
PROFIT (EUR MN)	**1**	**1**	**1**	**2**	**3**	**4**	**4**	**12**	**5**	**5**	**9**

JAPAN & ASIA PACIFIC (MEIJI SEIKA PARTNER EISAI)	**2020E**	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**
NUMBER OF PATIENTS	299,580	305,572	311,683	317,917	324,275	330,761	337,376	344,123	351,006	358,026	365,186
GROWTH (%)	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%
PATIENTS ON MEDICATION (%)	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%
PATIENTS TREATED	239,664	244,457	249,346	254,333	259,420	264,608	269,901	275,299	280,805	286,421	292,149
-/- PATIENTS WITH PD-LID	46,015	46,936	47,875	48,832	49,809	50,805	51,821	52,857	53,914	54,993	56,093
PATIENTS TREATED WITHOUT PD-LID	193,649	197,522	201,472	205,501	209,611	213,804	218,080	222,441	226,890	231,428	236,057
PENETRATION (%)	1.0%	1.5%	1.8%	2.3%	2.8%	3.3%	3.8%	3.9%	4.0%	2.8%	1.4%
NUMBER OF TREATED PATIENTS	1,936	2,963	3,626	4,727	5,869	7,056	8,287	8,675	9,076	6,480	3,305
COST OF THERAPY PER YEAR (EUR)	1,460	1,460	1,460	1,460	1,460	1,460	1,460	1,460	1,460	1,460	1,460
SALES (EUR MN)	**3**	**4.3**	**5**	**7**	**9**	**10**	**12**	**13**	**13**	**9**	**5**
CHANGE (%)		53%	22%	30%	24%	20%	17%	5%	5%	-29%	-49%
ROYALTY (%)	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%
ROYALTIES (EUR MN)	0.1	0.1	0.1	0.2	0.2	0.3	0.3	0.3	0.3	0.2	0.1
UPFRONT & MILESTONE PAYMENTS (EUR MN)	0										
PROFIT BEFORE TAX (EUR MN)	**0.1**	**0.1**	**0.1**	**0.2**	**0.2**	**0.3**	**0.3**	**0.3**	**0.3**	**0.2**	**0.1**
TAXES (EUR MN)	0	0	0	0	0	0	0	0	0	0	0
PROFIT (EUR MN)	**0.1**	**0.1**	**0.1**	**0.1**	**0.2**	**0.2**	**0.2**	**0.2**	**0.2**	**0.2**	**0.1**

	2020E	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**
GLOBAL SALES (EUR MN)	**57**	**67**	**79**	**99**	**140**	**171**	**196**	**212**	**227**	**195**	**155**
CHANGE (%)	16%	17%	17%	26%	42%	22%	14%	9%	7%	-14%	-21%
GLOBAL PROFIT (EUR MN)	**5**	**7**	**8**	**8**	**13**	**13**	**15**	**23**	**17**	**14**	**14**
CHANGE (%)	-25%	32%	9%	7%	62%	-2%	14%	56%	-25%	-18%	-3%

WACC (%)	7%
NPV TOTAL PROFIT (CHF MN)	**97**
NUMBER OF SHARES (MN)	17.8
NPV PER SHARE (EUR)	5.1
NPV PER SHARE (CHF)	5.4
SUCCESS PROBABILITY	100%
NPV PER SHARE (CHF)	**5.4**

SENSITIVITY ANALYSIS

		WACC (%)				
	CHF/SHARE	6.0	6.5	7.0	7.5	8.0
	380	9.5	9.2	9.0	8.8	8.5
	330	8.2	8.0	7.8	7.6	7.4
	280	7.0	6.8	6.6	6.5	6.3
PEAK SALES	230	5.7	5.6	**5.4**	5.3	5.2
	180	4.5	4.4	4.3	4.1	4.0
	130	3.2	3.2	3.1	3.0	2.9
	80	2.0	1.9	1.9	1.8	1.8

ESTIMATES AS OF 5 MAY 2021

SOURCE: VALUATIONLAB ESTIMATES

XADAGO (SAFINAMIDE) - FINANCIAL FORECASTS FOR PD-LID (LEVODOPA-INDUCED DYSKINESIA)

INDICATION	ADD ON THERAPY TO LEVODOPA/CARBIDOPA OR IN COMBINATION WITH OTHER PARKINSON'S DISEASE DRUGS IN MID-TO-LATE STAGE PATIENTS TO TREAT DYSKINESIA
DOSAGE	50 OR 100 MG / DAY
PRICE	EUROPE/ROW: EUR 2.80 PER DAY; US: USD 10 PER DAY; JAPAN: EUR 4 PER DAY
STANDARD OF CARE	ADAMAS' GOCOVRI (AMANTADINE ER) FIRST TREATMENT SPECIFICALLY APPROVED FOR PD-LID BUT HAMPERED WITH SAFETY AND TOLERABILITY ISSUES
UNIQUE SELLING POINT	ONCE DAILY ADD-ON THERAPY FOR PATIENTS WITH PD-LID WITH SUPERIOR SAFETY AND TOLERABILITY PROFILE

7Ps ANALYSIS

PATENT	PROTECTION EU (2029), US (2031): LEVODOPA COMBO PATENT 2026 (US) / 2024 (EU) + UP TO 5 YEAR EXTENSION I SYNTHESIS PATENT: 2027 I ANDA FILING REPORTED MAY 2021
PHASE	POTENTIALLY SINGLE PIVOTAL TRIAL IN PD-LID DESIGN AGREED WITH US, EU, ROW REGULATORS; TRIAL START Q1 2022, 2 YEAR TRIAL DURATION, LAUNCH 2024
PATHWAY	PD-LID IS A RECOGNIZED ORPHAN DRUG INDICATION IN THE US ELIGIBLE FOR 7 YEARS ORPHAN DRUG EXCLUSIVITY, FAST TRACK DESIGNATION WITH PRIORITY REVIEW
PATIENT	IMPROVING QUALITY OF LIFE BY REDUCING DYSKINESIA RELATED TO LONG-TERM LEVODOPA USE
PHYSICIAN	WELL TOLERATED AND SAFE TREATMENT THAT EFFECTIVELY REDUCES DYSKINESIA RELATED TO LONG-TERM LEVODOPA USE
PAYER	DELAYS SIGNIFICANT COSTS RELATED TO DYSKINESIA AND "WEARING OFF" WHERE PATIENTS NEED EXTENSIVE CARE OR HAVE TO BE INSTITUTIONALIZED
PARTNER	ZAMBON (WORLDWIDE EXCL. JAPAN & KEY ASIAN MARKETS), MEIJI SEIKA (JAPAN & KEY ASIAN MARKETS) - NEWRON SHARES IN MILESTONE & ROYALTY PAYMENTS

REVENUE MODEL

EUROPE / REST OF WORLD (ZAMBON & PARTNERS)	**2020E**	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**
NUMBER OF PATIENTS (MN)	3.8	3.9	3.9	4.0	4.1	4.2	4.3	4.3	4.4	4.5	4.6
GROWTH (%)	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%
PERCENTAGE DIAGNOSED (%)	70%	70%	70%	70%	70%	70%	70%	70%	70%	70%	70%
PATIENTS DIAGNOSED (MN)	2.6	2.7	2.8	2.8	2.9	2.9	3.0	3.0	3.1	3.2	3.2
PATIENTS TREATED WITH LEVODOPA (%)	60%	60%	60%	60%	60%	60%	60%	60%	60%	60%	60%
PATIENTS TREATED WITH LEVODOPA	1,587,131	1,618,873	1,651,251	1,684,276	1,717,961	1,752,321	1,787,367	1,823,114	1,859,577	1,896,768	1,934,704
MID TO LATE STAGE PATIENTS (%)	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%
MID TO LATE STAGE PATIENTS	1,269,705	1,295,099	1,321,001	1,347,421	1,374,369	1,401,856	1,429,894	1,458,491	1,487,661	1,517,415	1,547,763
MID TO LATE STAGE PATIENTS WITH PD-LID (%)	40%	40%	40%	40%	40%	40%	40%	40%	40%	40%	40%
PATIENTS WITH PD-LID	507,882	518,039	528,400	538,968	549,748	560,743	571,957	583,397	595,065	606,966	619,105
PENETRATION (%)	0%	0%	0%	0%	1%	2%	3%	4%	5%	5%	3%
NUMBER OF TREATED PATIENTS	0	0	0	0	8,590	35,046	53,621	72,925	83,681	89,148	63,652
COST OF THERAPY PER YEAR (EUR)	1,022	1,022	1,022	1,022	1,022	1,022	1,022	1,022	1,022	1,022	1,022
SALES (EUR MN)	**0**	**0**	**0**	**0**	**9**	**36**	**55**	**75**	**86**	**91**	**65**
CHANGE (%)						308%	53%	36%	15%	7%	-29%
ROYALTY (%)	10%	12%	12%	12%	14%	14%	14%	14%	14%	14%	14%
ROYALTIES (EUR MN)	0	0	0	0	1	5	8	10	12	13	9
UPFRONT & MILESTONE PAYMENTS (EUR MN)				4							
R&D COSTS (EUR MN)	-0.4	-2	-4	-3	0	0	0	0	0	0	0
PROFIT BEFORE TAX (EUR MN)	**0**	**-2**	**-4**	**1**	**1**	**5**	**8**	**10**	**12**	**13**	**9**
TAXES (EUR MN)	0	0	0	0	0	-2	-2	-3	-4	-4	-3
PROFIT (EUR MN)	**0**	**-2**	**-4**	**1**	**1**	**3**	**5**	**7**	**8**	**9**	**6**

UNITED STATES (ZAMBON PARTNER SUPERNUS PHARMA)	**2020E**	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**
NUMBER OF PATIENTS (MN)	1.2	1.2	1.3	1.3	1.3	1.3	1.4	1.4	1.4	1.5	1.5
GROWTH (%)	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%
PERCENTAGE DIAGNOSED (%)	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%
PATIENTS DIAGNOSED (MN)	1.0	1.0	1.0	1.0	1.1	1.1	1.1	1.1	1.1	1.2	1.2
PATIENTS TREATED WITH LEVODOPA (%)	60%	60%	60%	60%	60%	60%	60%	60%	60%	60%	60%
PATIENTS TREATED WITH LEVODOPA	585,117	596,820	608,756	620,931	633,350	646,017	658,937	672,116	685,558	699,269	713,255
MID TO LATE STAGE PATIENTS (%)	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%
MID TO LATE STAGE PATIENTS	468,094	477,456	487,005	496,745	506,680	516,813	527,150	537,693	548,447	559,415	570,604
MID TO LATE STAGE PATIENTS WITH PD-LID (%)	40%	40%	40%	40%	40%	40%	40%	40%	40%	40%	40%
PATIENTS WITH PD-LID	187,238	190,982	194,802	198,698	202,672	206,725	210,860	215,077	219,379	223,766	228,242
PENETRATION (%)	0%	0%	0%	0%	1%	3%	4%	5%	6%	6%	6%
NUMBER OF TREATED PATIENTS	0	0	0	0	4,433	19,381	26,357	33,606	37,706	38,460	39,229
COST OF THERAPY PER YEAR (EUR)	2,876	2,756	2,756	2,756	2,756	2,756	2,756	2,756	2,756	2,756	2,756
SALES (EUR MN)	**0**	**0**	**0**	**0**	**12**	**53**	**73**	**93**	**104**	**106**	**108**
CHANGE (%)						337%	36%	28%	12%	2%	2%
ROYALTY (%)	7.5%	7.5%	7.5%	7.5%	8.0%	8.0%	8.0%	8.0%	8.0%	8.0%	8.0%
ROYALTIES (EUR MN)	0	0	0	0	1	4	6	7	8	8	9
PROFIT BEFORE TAX (EUR MN)	**0**	**0**	**0**	**0**	**1**	**4**	**6**	**7**	**8**	**8**	**9**
TAXES (EUR MN)	0	0	0	0	0	-1	-2	-2	-3	-3	-3
PROFIT (EUR MN)	**0**	**0**	**0**	**0**	**1**	**3**	**4**	**5**	**6**	**6**	**6**

JAPAN & ASIA PACIFIC (MEIJI SEIKA PARTNER EISAI)	**2020E**	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**
NUMBER OF PATIENTS	299,580	305,572	311,683	317,917	324,275	330,761	337,376	344,123	351,006	358,026	365,186
GROWTH (%)	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%
PATIENTS WITH PD-LID	46,015	46,936	47,875	48,832	49,809	50,805	51,821	52,857	53,914	54,993	56,093
PENETRATION (%)	0%	0%	0%	0%	0%	1%	2%	3%	4%	4%	3%
NUMBER OF TREATED PATIENTS	0	0	0	0	0	794	3,239	4,955	6,402	6,359	4,540
COST OF THERAPY PER YEAR (EUR)	1,460	1,460	1,460	1,460	1,460	1,460	1,460	1,460	1,460	1,460	1,460
SALES (EUR MN)	**0**	**0**	**0**	**0**	**0**	**1**	**5**	**7**	**9**	**9**	**7**
CHANGE (%)							308%	53%	29%	-1%	-29%
ROYALTY (%)	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%
ROYALTIES (EUR MN)	0	0	0	0	0	0	0	0	0	0	0
PROFIT BEFORE TAX (EUR MN)	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
TAXES (EUR MN)	0	0	0	0	0	0	0	0	0	0	0
PROFIT (EUR MN)	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**

	2020E	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**
GLOBAL SALES (EUR MN)	**0**	**0**	**0**	**0**	**21**	**90**	**132**	**174**	**199**	**206**	**180**
CHANGE (%)						330%	46%	32%	14%	4%	-13%
GLOBAL PROFIT (EUR MN)	**0**	**-2**	**-4**	**1**	**2**	**6**	**9**	**12**	**14**	**15**	**12**
CHANGE (%)	-60%	400%	90%	-121%	129%	244%	46%	33%	14%	5%	-17%
WACC (%)	7%										
NPV TOTAL PROFIT (CHF MN)	**46**										
NUMBER OF SHARES (MN)	17.8										
NPV PER SHARE (CHF)	3										
SUCCESS PROBABILITY	15%	(PROOF-OF-CONCEPT ESTABLISHED)									
RISK ADJUSTED NPV PER SHARE (CHF)	**0.4**										

SENSITIVITY ANALYSIS

		WACC (%)				
	CHF/SHARE	6.0	6.5	7.0	7.5	8.0
	65%	1.8	1.7	1.7	1.6	1.5
	55%	1.5	1.5	1.4	1.4	1.3
	45%	1.2	1.2	1.2	1.1	1.1
SUCCESS PROBABILITY	35%	1.0	0.9	0.9	0.9	0.8
	25%	0.7	0.7	0.6	0.6	0.6
	15%	0.4	0.4	**0.4**	0.4	0.4
	5%	0.1	0.1	0.1	0.1	0.1

ESTIMATES AS OF 5 MAY 2021

SOURCE: VALUATIONLAB ESTIMATES

Unique Selling Point

Once daily oral add-on therapy given together with levodopa in Parkinson's patients with mid- to late-stage disease, with a unique dual mechanism of action. Xadago reduces levodopa dose and increases "on-time" without troublesome dyskinesia with proven safety and efficacy over a 2-years treatment period. The potential to reduce dyskinesia owing to Xadago's unique dual mechanism will be addressed in the upcoming PD-LID trial.

7P's Analysis

Patent: Granted combination patents protect Xadago until 2024 in the EU and 2026 in the US with a likely 5-year patent extension. A synthesis patent protects until 2027. We assume patent protection in both regions up to 2029. In May 2021, Newron reported a generic manufacturer filed a Paragraph IV ANDA for Xadago in the US, which could lead to generics entering the US market earlier than expected.

Phase: Launched in the EU in early 2015, in the lucrative US market in 2017 and in Japan in 2019. A new, global trial in PD-Lid is expected to start in Q1 2022 (delayed by Covid-19 pandemic) with first approvals in this orphan indication expected in 2024.

Pathway: To receive US approval, Xadago needed at least one positive phase III trial for each Parkinson's indication (early and mid-to late-stage disease), at least 1,500 patients treated with Xadago of which several hundred treated for six months and at least 100 treated for one year. Newron comfortably fulfilled these requirements with two positive phase III trials and more than 1,500 patients treated with Xadago leading to US approval in March 2017

Patient: The major benefit for patients is that they can shift back the use of mainstay levodopa that causes irreversible side effects related to long-term use of this drug. In early disease, Xadago in combination with dopamine agonists helps improve motor fluctuations. Furthermore, in late stage patients, improvement is seen of multiple domains without any increase in troublesome dyskinesia.

Physician: Xadago adds a new treatment option for Parkinson's disease that fits nicely in current levodopa-sparing treatment strategies with the aim to reduce the burden of the long-term side effects from this effective drug. Potential anti-dyskinetic effects of Xadago would add to the use of the drug (will be addressed in potentially pivotal PD-LID trial).

Payer: The largest share of direct costs in Parkinson's comes from inpatient care and nursing homes, while the share from medication is substantially lower. Any delay in the progression of the disease or reduced debilitating side effects, in particular dyskinesia, has a substantial impact on total treatment costs.

Partner: Zambon acquired the global rights (excluding Japan & Asian territories owned by Meiji Seika) for Xadago in May 2012. Zambon has a strong presence in Southern Europe, France and Latin America, where it markets the drug. Supernus Pharma will now commercialize Xadago in the US after it acquired the CNS portfolio of US WorldMeds, including Xadago, in April 2020. Meiji Seika has Japanese & Asian rights, which were sublicensed to Eisai for certain Asian territories in 2017. Newron and Zambon will share the costs of the PD-LID trial equally. Newron will qualify for a one-time milestone payment and a greater share of royalties on overall Zambon sales should the trial lead to a label extension.

Parkinson's Disease Market

Parkinson's disease is the second most common neurodegenerative disorder after Alzheimer's disease. Nevertheless, the Parkinson's disease market is relatively small in terms of sales at around USD 4 bn, reflecting the lack of new efficacious treatment introductions, with most drugs no longer patent protected. Major players included Novartis, Bristol-Myers Squibb and GlaxoSmithKline. Several smaller players have developed new formulations (extended/controlled-release, patches, orally disintegrating tablets) extending the patent life of some existing branded drugs. The combined direct (medication, inpatient care) and indirect cost (inability to work) of Parkinson's disease is estimated to be nearly USD 25 bn per year in the US alone.

PARKINSON'S DISEASE - KEY FACTS	
MARKET SIZE	USD 4 BN
PREVALENCE	7-10 MN GLOBALLY, 1 MN IN US, > 1 MN IN EU
INCIDENCE	300,000 GLOBALLY, 100,000 IN US, >100,000 IN EU; 0.3% OF POPULATION
UNDERLYING CAUSE	- LOSS AND DEGENERATION OF DOPAMINERGIC NEURONS IN STRIATA NIGRA - LOSS OF STRATIAL NEUROTRANSMITTER DOPAMINE
SYMPTOMS	- TREMOR (SHAKING OF HANDS, ARMS, LEGS, JAW, FACE) - RIGIDITY (LIMBS, TRUNK) - BRADYKINESIA (SLOWNESS OF MOVEMENT) - POSTURAL INSTABILITY (POOR BALANCE AND COORDINATION)
DRUG CLASS (KEY BRANDS)	- LEVODOPA/CARBIDOPA (MADOPAR, SINEMET CR, PARCOPA, STALEVO, DUODOPA) - DOPAMINE AGONIST (MIRAPEX, REQUIP, APOKYN, PARLODEL, NEUPRO PATCH) - MAO-B INHIBITORS (AZILECT, ELDEPRYL, ZELAPAR ODT, XADAGO) - COMT INHIBITORS (COMTAN, TASMAR) - ANTICHOLINERGICS (COGENTIN, ARTANE) - OTHER (SYMMETREL FOR DYSKINESIA, EXELON FOR DEMENTIA)
MAJOR PLAYERS (KEY BRANDS)	- NOVARTIS (STALEVO, PARLODEL, COMTAN) - BRISTOL MYERS SQUIBB (SINEMET CR) - GLAXOSMITHKLINE (REQUIP) - TEVA (AZILECT) - UCB (NEUPRO PATCH) - BOEHRINGER INGELHEIM (MIRAPEX ER) - US WORLDMEDS (APOKYN, XADAGO) - VALEANT (ZELAPAR ODT, TASMAR) - ABBVIE (DUODOPA) - ENDO PHARMACEUTICALS (SYMMETREL) - ZAMBON/MEIJI SEIKA (XADAGO)

SOURCE: VALUATIONLAB, NIH, WHO, PARKINSONS.ORG, PDF.ORG, COMPANY REPORTS

Parkinson's disease affects an estimated 7-10 million people globally with about 1 million patients in the US and a similar amount in the EU, with significant prevalence growth expected due to an aging population. The disease is a slowly progressive degenerative disorder of the central nervous system that initially affects movement, and later cognition and behavior. Dementia commonly occurs in the advanced stage of disease. The mean age of onset is typically around 60 years (rare in people under the age of 40 years). In people taking medication (levodopa), the progression time of symptoms to a stage of high dependency from caregivers may range from 8 to 15 years.

Three stages of severity are usually distinguished;

1) **Early stage**, in which the patient has developed some disability and where drug treatment may be required (dopamine agonists, anticholinergics, MAO-B inhibitors)
2) **Mid stage**, where the symptoms can be rather severe and include the inability to walk straight or stand, with a noticeable slowing of movements (bradykinesia).
3) **Late or advanced stage**, in which an individual develops severe motor complications (dyskinesia) related to levodopa use. Most patients are unable to complete day-to-day tasks and usually cannot live on their own.

Early in the disease the most obvious symptoms are movement-related. These include tremor, rigidity, slowness of movement, and difficulty with walking and gait. The motor symptoms of the disease result from the death of dopamine-generating cells in the

substantia nigra, a small tract of neurons in the brain containing dopamine, which control voluntary movements. The cause of this cell death is still unknown.
The severity and progression of Parkinson's disease is measured using several rating scales such as the Hoehn and Yahr (focus on movement symptoms) or **UPDRS** (United Parkinson's Disease Rating Scale - more comprehensive than Hoehn and Yahr, taking into account cognitive difficulties, daily activities and treatment complications).

Current drug treatment aims to delay symptoms and use of levodopa
Because there is no cure for Parkinson's disease, the primary aim of treatment is to relieve symptoms and keep the patient functional as long as possible. Current treatments are effective at managing the early motor symptoms, mainly through the use of (generic) levodopa and dopamine agonists. Mainstay treatment is levodopa, an oral precursor of the neurotransmitter dopamine. It is well established as the most effective treatment for Parkinson's disease for over 30 years, with most patients noticing an immediate improvement. However, as the disease progresses and dopamine generating cells continue to be lost, these drugs eventually become ineffective at treating the symptoms and at the same time produce **dyskinesia**, a complication marked by involuntary jerking and twisting movements. Other treatment related complications include end-of-dose deterioration, unpredictable "on/off" motor fluctuations, hypotension, nausea, anorexia and psychiatric effects. These problems have led to the development of strategies that aim to limit or delay the onset of levodopa-related complications and have become the key drivers for the Parkinson's disease market with the introduction of dopamine agonists, MOA-B and COMT inhibitors. Dopamine agonists and MAO-B inhibitors are primarily used as mono-therapy in the early stages of the disease to delay the use of levodopa. **Dopamine agonists** work by directly stimulating the dopamine receptors to bypass degenerating brain cells. **MOA-B inhibitors** block a key enzyme that is responsible for the breakdown of dopamine. **COMT-inhibitors** block an enzyme responsible for the breakdown of levodopa in the body, thereby increasing the amount of levodopa available to reach the brain. Consequently, COMT inhibitors are prescribed together with levodopa. When drug treatment is no longer sufficient to control symptoms, lesional surgery or deep brain stimulation (DBS), through implantation of a so-called brain pacemaker can be of use. In the final stages of disease, palliative care is provided to enhance quality of life.

New market entrants expected to spark growth
The introduction of new drugs, improved formulations of existing drugs, and the ageing of the population (higher prevalence) should drive growth in the Parkinson’s disease market.

Improved formulations of existing drugs, including: Abbvie's **Duodopa**, a carbidopa/levodopa intestinal gel (approved), Impax’s **Rytary**, an extended-release capsule formulation of carbidopa/levodopa (approved), and NeuroDerm's **ND0612L/H**, a carbidopa/levodopa subcutaneous patch pump (phase II), Mylan’s/US WorldMeds’ **Apokyn**, a non-ergoline dopamine agonist for the treatment of acute hypomobility (approved), and Adamas’ **Gocovri** (sustained-release formulation of amantadine) for treating PD-LID (approved).

New molecules and novel approaches, including: Newron/Zambon's **Xadago** (approved in EU & US) a dual mechanism of action drug that provides both MAO-B and glutamate inhibition, adenosine 2a (A2a) agonists such as Kyowa-Kirin's **istradefylline** (global phase III did not meet primary endpoint, Japan approved as Nouriast) and Addex's **dipraglurant** (phase II), which targets metabotropic glutamate receptor 5 (mGluR5).

Income Statement

NEWRON PHARMACEUTICALS									SHARE PRICE (CHF)	2.2	
IFRS											
INCOME STATEMENT (EUR MN)	2020	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E
PRODUCT SALES (INCLUDING PARTNERS)	**57**	**67**	**79**	**99**	**190**	**597**	**896**	**1,128**	**1,279**	**1,395**	**1,447**
CHANGE (%)	16%	17%	17%	26%	92%	215%	50%	26%	13%	9%	4%
PRODUCT SALES (BY NEWRON)	**0**	**0**	**0**	**0**	**3**	**20**	**33**	**45**	**55**	**57**	**58**
CHANGE (%)						509%	69%	35%	22%	4%	3%
ROYALTIES	**5**	**7**	**8**	**10**	**23**	**91**	**142**	**181**	**205**	**229**	**244**
CHANGE (%)	10%	33%	15%	25%	128%	299%	55%	27%	14%	12%	6%
LICENCE, UPFRONT & MILESTONE INCOME	**0**	**0**	**23**	**69**	**23**	**0**	**0**	**60**	**0**	**0**	**84**
OTHER INCOME & GRANTS	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
REVENUES (EXCL. PARTNER SALES)	**5**	**7**	**31**	**79**	**49**	**111**	**175**	**285**	**260**	**286**	**385**
CHANGE (%)	-25%	32%	352%	152%	-38%	124%	58%	63%	-9%	10%	35%
COGS	**0**	**0**	**0**	**0**	**0**	**-3**	**-5**	**-7**	**-8**	**-8**	**-9**
GROSS PROFIT	**5**	**7**	**31**	**79**	**49**	**108**	**170**	**279**	**251**	**277**	**376**
CHANGE (%)	-25%	32%	352%	152%	-38%	120%	58%	64%	-10%	10%	36%
MARGIN	100%	100%	100%	100%	99%	97%	97%	98%	97%	97%	98%
R&D	**-15**	**-14**	**-21**	**-18**	**-15**	**-12**	**-12**	**-13**	**-13**	**-14**	**-15**
CHANGE (%)	-15%	-6%	50%	-14%	-17%	-23%	5%	5%	5%	5%	5%
S,G&A	**-8**	**-8**	**-8**	**-8**	**-16**	**-18**	**-18**	**-19**	**-19**	**-19**	**-20**
CHANGE (%)	-19%	0%	-6%	0%	105%	8%	1%	7%	-1%	2%	1%
OPERATING EXPENSES	**-23**	**-22**	**-29**	**-26**	**-32**	**-32**	**-35**	**-39**	**-40**	**-42**	**-43**
CHANGE (%)	-17%	-4%	29%	-10%	23%	1%	9%	10%	5%	3%	3%
AS % REVENUES	444%	324%	92%	33%	64%	29%	20%	14%	16%	15%	11%
EBITDA	**-18**	**-15**	**3**	**53**	**18**	**79**	**140**	**247**	**219**	**244**	**342**
CHANGE (%)	-14%	-14%	-117%	1938%	-67%	341%	78%	76%	-11%	11%	40%
MARGIN (%)	-339%	-220%	8%	67%	36%	71%	80%	87%	85%	85%	89%
DEPRECIATION & AMORTIZATION	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
AS % REVENUES	4%	3%	1%	0%	1%	0%	0%	0%	0%	0%	0%
EBIT	**-18**	**-16**	**2**	**53**	**18**	**79**	**140**	**247**	**219**	**244**	**342**
CHANGE (%)	-14%	-14%	-115%	2134%	-67%	346%	78%	76%	-11%	11%	40%
MARGIN (%)	-344%	-224%	8%	67%	36%	71%	80%	86%	84%	85%	89%
NET FINANCIAL INCOME/(EXPENSE)	**-2**	**-2**	**-2**	**-2**	**0**	**1**	**2**	**3**	**4**	**5**	**6**
PROFIT BEFORE TAXES	**-20**	**-17**	**1**	**52**	**18**	**80**	**142**	**249**	**223**	**249**	**348**
MARGIN	-373%	-246%	3%	65%	36%	72%	81%	87%	86%	87%	90%
TAXES	**-1**	**-1**	**-2**	**-14**	**-7**	**-32**	**-52**	**-89**	**-77**	**-85**	**-118**
TAX RATE (%)	-7%	-8%	247%	27%	40%	40%	36%	36%	35%	34%	34%
NET PROFIT/LOSS	**-21**	**-18**	**-1**	**38**	**10**	**47**	**90**	**161**	**146**	**164**	**231**
CHANGE (%)	4%	-12%	-93%	-3195%	-72%	352%	90%	79%	-9%	12%	41%
MARGIN (%)	-399%	-266%	-4%	48%	21%	43%	52%	56%	56%	57%	60%
PROFIT/(LOSS) PER SHARE (IN EUR)	**-1.18**	**-1.03**	**-0.07**	**2.12**	**0.59**	**2.66**	**5.05**	**9.02**	**8.17**	**9.17**	**12.92**
PROFIT/(LOSS) PER SHARE (IN CHF)	**-1.26**	**-1.15**	**-0.08**	**2.35**	**0.65**	**2.94**	**5.60**	**9.99**	**9.05**	**10.16**	**14.31**

ESTIMATES AS OF 5 MAY 2021 SOURCE: VALUATIONLAB ESTIMATES

NOTE: At the end of FY 2020 Newron had a total of EUR 244.3 mn tax loss carryforwards, which we anticipate the company will be able to use on future profits.

Timelines and forecasts may be affected by the COVID-19 pandemic.

Ratios & Balance Sheet

NEWRON PHARMACEUTICALS									SHARE PRICE (CHF)	2.2	
RATIOS	**2020**	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**
P/E		**-1.9x**	**-28.4x**	**0.9x**	**3.3x**	**0.7x**	**0.4x**	**0.2x**	**0.2x**	**0.2x**	**0.2x**
P/S		**5.0x**	**1.1x**	**0.4x**	**0.7x**	**0.3x**	**0.2x**	**0.1x**	**0.1x**	**0.1x**	**0.1x**
P/NAV		**-28.6x**	**-14.2x**	**1.0x**	**0.8x**	**0.4x**	**0.2x**	**0.1x**	**0.1x**	**0.1x**	**0.0x**
EV/EBITDA		**-0.2x**	**1.3x**	**0.1x**	**0.2x**	**0.0x**	**0.0x**	**0.0x**	**0.0x**	**0.0x**	**0.0x**
PER SHARE DATA (CHF)	**2020**	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**
EARNINGS	**-1.26**	**-1.15**	**-0.08**	**2.35**	**0.65**	**2.94**	**5.60**	**9.99**	**9.05**	**10.16**	**14.31**
CHANGE (%)	1%	-9%	-93%	-3195%	-72%	352%	90%	79%	-9%	12%	41%
CASH	**1.87**	**2.21**	**2.66**	**6.35**	**8.01**	**13.58**	**23.10**	**39.38**	**54.07**	**70.45**	**93.09**
CHANGE (%)	-22%	18%	21%	138%	26%	70%	70%	70%	37%	30%	32%
DIVIDENDS	**0.00**	**0.00**	**0.00**	**0.00**	**0.00**	**0.00**	**0.00**	**0.00**	**0.00**	**0.00**	**0.00**
PAYOUT RATIO (%)	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
NET ASSET VALUE	**1.03**	**-0.08**	**-0.15**	**2.19**	**2.84**	**5.79**	**11.38**	**21.37**	**30.42**	**40.58**	**54.89**
CHANGE (%)	-54%	-107%	101%	-1553%	30%	103%	97%	88%	42%	33%	35%
BALANCE SHEET (EUR MN)	**2020**	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**
NET LIQUID FUNDS	**31**	**36**	**43**	**102**	**129**	**219**	**372**	**634**	**871**	**1,135**	**1,500**
TOTAL ASSETS	**51**	**55**	**63**	**122**	**149**	**239**	**392**	**654**	**891**	**1,155**	**1,520**
SHAREHOLDERS' EQUITY	**17**	**-1**	**-2**	**35**	**46**	**93**	**183**	**344**	**490**	**654**	**884**
CHANGE (%)	-53%	-107%	101%	-1553%	30%	103%	97%	88%	42%	33%	35%
RETURN ON EQUITY (%)	-122%	1524%	50%	107%	23%	51%	49%	47%	30%	25%	26%
FINANCIAL DEBT	**26**	**41**	**41**	**41**	**31**	**21**	**11**	**0**	**0**	**0**	**0**
FINANCIAL DEBT AS % OF TOTAL ASSETS	50%	73%	65%	33%	21%	9%	3%	0%	0%	0%	0%
EMPLOYEES	**24**	**24**	**24**	**24**	**24**	**24**	**24**	**24**	**24**	**24**	**24**
CHANGE (%)	-8%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
CASH FLOW STATEMENT (EUR MN)	**2020**	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**
NET PROFIT / (LOSS) BEFORE TAX	-20	-17	1	52	18	80	142	249	223	249	348
DEPRECIATION & AMORTIZATION	0	0	0	0	0	0	0	0	0	0	0
OTHER NON-CASH ITEMS	0	2	2	2	2	2	2	2	2	2	2
CASH FLOW	**-19**	**-15**	**3**	**54**	**20**	**82**	**144**	**252**	**225**	**251**	**351**
NET INCREASE/(DECREASE) IN WORKING CAPITAL	4	4	4	4	5	5	5	5	6	6	6
OPERATING FREE CASH FLOW	**-16**	**-11**	**7**	**59**	**27**	**90**	**153**	**262**	**237**	**264**	**365**
NET CASH FLOWS FROM INVESTING ACTIVITIES	-1	0	0	0	0	0	0	0	0	0	0
NET CASH USED IN OPERATING ACTIVITIES	**-16**	**-11**	**7**	**59**	**27**	**90**	**153**	**262**	**237**	**264**	**365**
NET CASH FLOWS FROM FINANCING ACTIVITIES	7	15	0	0	0	0	0	0	0	0	0
NET INCREASE/(DECREASE) CASH & CASH EQUIVALENTS	**-9**	**4**	**7**	**59**	**27**	**90**	**153**	**262**	**237**	**264**	**365**

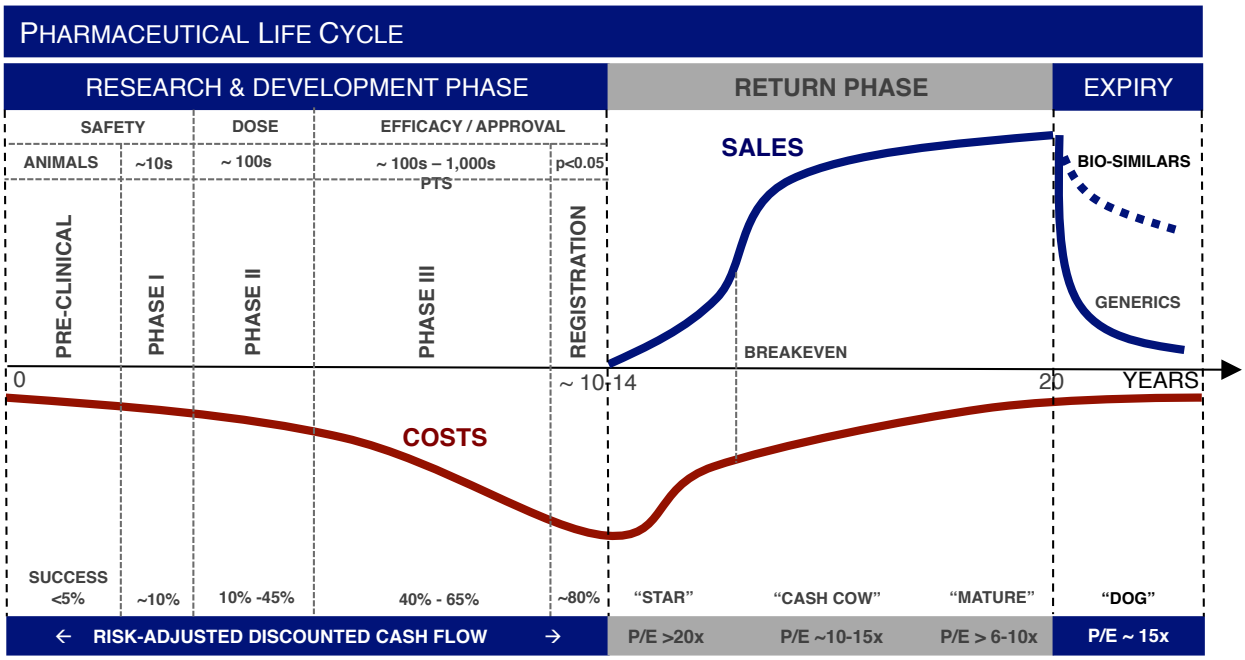
ESTIMATES AS OF 5 MAY 2021 — SOURCE: VALUATIONLAB ESTIMATES

NOTE: With cash and cash equivalents of EUR 31.3 mn (31 December 2020), a remaining undrawn EUR 15 mn from the EUR 40 mn EIB loan, increasing royalty income from Xadago sales and Italian R&D tax credits, Newron expects to have sufficient funds for its operations and development programs into early 2023.

APPENDIX

Pharmaceutical life cycle

To determine the value of a prescription (bio)pharmaceutical compound, it is critical to understand its life cycle. Fortunately, all compounds follow the same life cycle. The clock starts ticking after the compound is patented, providing 20 years of protection from generic competition. Market exclusivities can extend this protection period. The average Research & Development Phase takes 10-14 years, leading to an effective Return Phase of 6-10 years. The Development Phase has 3 distinct Phases, focused on safety (Phase I), dose (Phase II) and efficacy/clinical benefit (Phase III). The compound is filed for registration/approval at the FDA (US) or EMA (EU). The Return Phase is characterized by a star, cash cow, and mature phase. After patent expiry (or loss of market exclusivity) generic manufacturers may copycat the branded prescription drug, at significantly lower costs, leading to a sales and earnings implosion of the branded drug.



SOURCE: VALUATIONLAB

Success probabilities & Royalties

In our risk-adjusted NPV calculations, we use standardized success probabilities based on historical clinical success rates. The success rate increases as the project progresses through development. Sales and earnings forecasts are based on the clinical and competitive profile of the compound. The more advanced the compound is, the more accurate the forecasts become as the target market can be defined. We conservatively exclude projects that lack Phase IIa proof-of-concept data in our valuations.

SUCCESS PROBABILITIES & ROYALTIES

DEVELOPMENT STAGE	AIM	WHAT / WHO	SUCCESS PROBABILITY (%)	COSTS (USD MN)	ROYALTIES (%)
PRE-CLINICAL	SAFETY & PHARMACOLOGY DATA	LAB TESTS / ANIMALS - NO HUMANS!	< 5	3	
PHASE I	SCREENING FOR SAFETY	HEALTHY VOLUNTEERS (10'S)	5-15	3	< 5
PHASE IIA	PROOF-OF-CONCEPT	PATIENTS WITH DISEASE (10'S)	10-20		
PHASE II	ESTABLISH THE TESTING PROTOCOL	PATIENTS WITH DISEASE (100'S)	15-35	5	5-15
PHASE IIB	OPTIMAL DOSAGE	PATIENTS WITH DISEASE (100'S)	20-45	5-10	
PHASE III	EVALUATE OVERALL BENEFIT/RISK	PATIENTS WITH DISEASE (1,000'S)	40-65	> 20-1,000	10-25
REGULATORY FILING	DETERMINE PHYSICIAN LABELING	CLINICAL BENEFIT ASSESSMENT	80-90		
APPROVAL	MARKETING AUTHORIZATION	PHYSICIANS FREE TO PRESCRIBE	100		15-30

SOURCE: VALUATIONLAB, TUFTS, FDA, EMA, CLINICALTRIALS.GOV

Important Research Disclosures

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Our financial analyses are based on the "Directives on the Independence of Financial Research" issued by the Swiss Bankers Association in January 2008.

Purpose of the Research

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Risk Qualification

Speculative	less than 1 year cash and breakeven beyond 1 year
High Risk	profitable within 2 years and 1 approved product/key indication (patent expiry > 5 years)
Medium Risk	profitable and/or sales from at least 2 marketed products/key indications (patent expiry > 5 years)
Low Risk	profitable and sales from >2 marketed products/key indications (patent expiry > 5 years)

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