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)	134	**PRICE ON 25 MARCH 2024**	7.5
ENTERPRISE VALUE (CHF MN)	122	**RISK-ADJUSTED NPV PER SHARE** (CHF)	12.7
CASH (31 DECEMBER 2023) (CHF MN)	12	**UPSIDE/DOWNSIDE** (%)	69%
MONTHLY OPERATING EXPENSE (CHF MN)	1.4	**RISK PROFILE**	HIGH RISK
CASH RUNWAY (YEAR)	WELL INTO 2025	**SUCCESS PROBABILITY LEAD PIPELINE DRUG**	50%
BREAK-EVEN (YEAR)	2024*	**EMPLOYEES** (GROUP)	22
FOUNDED (YEAR)	1998	**LISTED** (YEAR)	2006
KEY PRODUCTS:	**STATUS**	**MAJOR SHAREHOLDERS:**	**(%)**
- XADAGO (PARKINSON'S DISEASE)	MARKETED	- ZAMBON GROUP	4.4
- EVENAMIDE (NON-TREATMENT-RESISTANT SCHIZOPHRENIA)	PHASE II/III	- EUROPEAN INVESTMENT BANK	3.7
- EVENAMIDE (TREATMENT-RESISTANT SCHIZOPHRENIA INCL. CTRS**)	POC ESTABLISHED	- EXECUTIVE MANAGEMENT	0.6
		- FREE FLOAT	99.4
		- AVERAGE TRADING VOLUME (30-DAYS)	155,098
UPCOMING CATALYSTS:	**DATE**	**ANALYST(S):**	BOB POOLER
- EVENAMIDE - TOPLINE RESULTS "STUDY 008A" IN NON-TRS^^ PATIENTS	APRIL 2024		BP@VALUATIONLAB.COM
- EVENAMIDE - PARTNERING AGREEMENT	BEFORE START "STUDY 017"		+41 79 652 67 68
- EVENAMIDE - START PIVOTAL "STUDY 017" IN TRS^ PATIENTS	Q3 2024		

* ASSUMES PARTNERING EVENAMIDE IN 2024; **CTRS = CLOZAPINE TREATMENT-RESISTANT SCHIZOPHRENIA; ^ TRS = TREATMENT-RESISTANT SCHIZOPHRENIA; ^^ NON-TRS (INADEQUATE RESPONDERS)

ESTIMATES AS OF 25 MARCH 2024

SOURCE: VALUATIONLAB ESTIMATES, NEWRON PHARMACEUTICALS

A pivotal year

Major catalysts: "Study 008A" results & partnering deal

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), and 2) evenamide, an add-on therapy for schizophrenia and treatment-resistant schizophrenia (TRS), including CTRS (clozapine treatment-resistant schizophrenia, an orphan-like indication). With cash and current financial assets of EUR 12.6 mn (31 December 2023), increasing Xadago revenues, Italian R&D tax credits, and a recent share subscription by an institutional healthcare investor, Newron sees a cash runway well into 2025. The company is adequately funded beyond its key value inflection points, including the first of two potentially pivotal phase II/III trials with evenamide in schizophrenia and TRS. We derive a sum-of-parts risk-adjusted (r)NPV value of CHF 12.7 per share, with 10% of the value related to Xadago, 86% to evenamide, and 4% to cash. Newron's risk profile is High Risk as the company is loss-making with revenues only from Xadago royalties in Parkinson's disease.

Key catalysts:

- **Results "Study 008A" of evenamide in non-TRS (April 2023):** the first, potentially pivotal, phase II/III trial of 30 mg evenamide twice-daily (BID) as add-on therapy in 291 schizophrenia patients who are inadequate responders to second-generation antipsychotics.
- **Partnering evenamide with a major CNS player (before starting "Study 017"**): Out-licensing evenamide to a major CNS player in return for substantial upfront, regulatory, and sales milestones and royalties on sales, extending the cash runway, which can be used to in-license new CNS compounds and sell evenamide in CTRS through a small in-house commercial team of key account managers in the US.
- **Start pivotal "Study 017" trial of evenamide in TRS (Q3 2024):** this marks the second potentially pivotal phase III trial needed for approval of evenamide in schizophrenia, including (clozapine) treatment-resistant schizophrenia; our success rate increases to 50% (phase II/III trial) from 35% (POC established) resulting in an increase of our rNPV by CHF 1.0 per share.

Investment case, strategy & cash

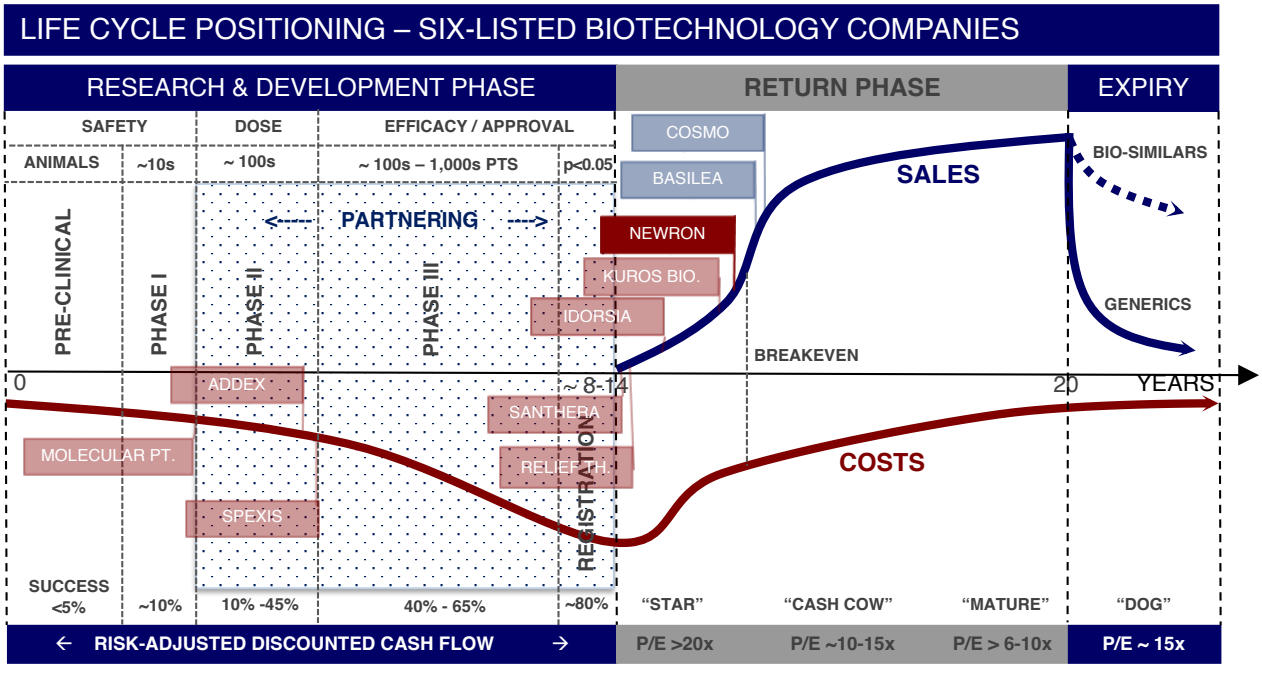
Investment case in a nutshell

Newron's key driver, evenamide for schizophrenia, continues to provide exciting data in treatment-resistant schizophrenia (TRS), with its phase II "Study 014/015" trial showing unprecedented efficacy results after one year of treatment. The company will submit these results and the protocol for the second pivotal "Study 017" (previously named "Study 003") trial in TRS patients to the FDA. The first pivotal "Study 008A of evenamide in inadequate responders to current antipsychotics will report topline results in April 2024; the second pivotal "Study 017" in TRS patients is planned to start in Q3 2024. Both should add significantly to the value while substantially increasing the success rate and reducing the clinical development risk. Upon positive results of "Study 008A" and on the back of the unprecedented results of "Study 014/015", a (global) partnering deal with a major CNS player is expected to be signed before the start of "Study 017" in Q3 2024, providing further equity upside. Hence, we believe substantial equity upside should be unlocked in 2024.

Based on our detailed bottom-up forecasts for Newron's key drivers, which have ample patent life and market exclusivity and target blockbuster markets, we conservatively calculate a sum-of-the-parts risk-adjusted NPV of CHF 227 mn or CHF 12.7 per share, providing equity upside of 69% from the current share price.

Life Cycle Positioning – High Risk

We qualify Newron's risk profile as High Risk as the company still makes losses, and revenues depend solely on Xadago in Parkinson's disease. On reaching breakeven in 2024 (assuming a significant agreement for evenamide in schizophrenia with substantial upfront payments) and the 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

Italian biopharmaceutical company specializing in CNS and rare diseases

Newron Pharmaceuticals S.p.A. is an Italian biopharmaceutical company specializing in prescription drugs to treat peripheral & central nervous system (CNS) disorders and rare, so-called orphan diseases, with 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 23 employees. Newron was listed on the SIX Swiss Stock Exchange 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 an optimal value, then out-license major indications and preferably market orphan indications by an own small specialist salesforce

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's pipeline consists of a nice mix of major indications, such as Xadago, which already generates revenues through its partners in Parkinson's disease, and evenamide as an add-on to antipsychotics in schizophrenia, and an orphan-like indication, such as evenamide in CTRS (clozapine treatment-resistant schizophrenia) with a high unmet medical need. Substantial value will be unlocked with the approval and launch of evenamide in schizophrenia with blockbuster sales potential. Newron's individual products include:

- **Evenamide – A 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. The compound is being developed as an add-on treatment for 1) non-treatment-resistant schizophrenia (non-TRS) patients experiencing inadequate response to current atypical antipsychotic monotherapy and 2) treatment-resistant schizophrenia (TRS) patients who are not responding adequately to any second-generation antipsychotics, including the orphan-like indication clozapine treatment-resistant schizophrenia (CTRS), covering roughly 70% of schizophrenia patients. Approximately 30% of schizophrenia patients respond well to monotherapy.

  Health authorities (Spain, Denmark, Sweden, Germany, UK, CHMP, US, Canada) have agreed with the current phase III development program for evenamide in schizophrenia. In 2021, Newron provided additional informative trials requested by the FDA before starting phase III development. The preclinical part of the safety work was completed and submitted to the FDA with no toxicity issues reported. The first 4-week clinical safety (EEG – electroencephalogram) trial dubbed "Study 008" in 138 patients was completed in March 2021, with no safety issues.

In January 2024, unprecedented topline results were presented of the open-label (unblinded) phase II "Study 014/015" safety and dose-ranging trial of evenamide (twice daily 7.5 mg, 15 mg, or 30 mg evenamide, no placebo) as an add-on to current antipsychotics (excluding clozapine) in 161 patients suffering from TRS. This was the final safety requirement by the FDA before starting phase III development in schizophrenia. Newron plans to start the potentially pivotal phase III "Study 017" trial (previously named "Study 003") of evenamide in TRS patients by the end of Q2 2024. Newron plans to recruit roughly 15-20% of clozapine treatment-resistant schizophrenia (CTRS) patients to address this orphan-like population. If the exceptional results seen in "Study 014/015" are replicated, approval of evenamide in TRS could follow swiftly based on this single pivotal trial alone. Evenamide could become the first drug for TRS since clozapine in 1989.

In September 2021, Newron started the first potentially pivotal phase II/III "Study 008A" trial of evenamide in 290 non-TRS patients in Europe, Asia, and Latin America. Topline results are expected to be reported in April 2024.

The company plans to out-license evenamide to global and/or local CNS players for substantial upfront, regulatory, and sales milestones and royalties on sales. This is expected to occur before the start of the pivotal "Study 017" in Q3 2024. Newron would like to commercialize evenamide in CTRS in the lucrative US market to optimize the long-term value, as limited marketing resources are required for this niche indication.

- **Xadago – First product to reach market – sales uptake hampered by generics**
  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. In 2021, several generic manufacturers filed Paragraph IV ANDA's for Xadago in the US. Newron and its partners Zambon and Supernus have reached a settlement agreement with the generic manufacturers, allowing them to enter the US market no earlier than 1 December 2027. Supplementary Protection Certificates (SPCs) have been approved in most major markets, and the company is confident these will be granted in all key territories, providing protection until 2029.

FY 2023 results in a nutshell – Topline boosted by Xadago revenues

FY 2023 revenue increased by +49% to EUR 9.1 mn, largely boosted by Xadago royalties up 13% to EUR 6.7 mn and a one-time jump in other income to EUR 2.3 mn. R&D expenditure increased by 10% to EUR 13.2 mn, S, G&A increased modestly by 2% to EUR 7.5 mn. A slightly lower net loss of EUR 16.2 mn was reported in 2023 compared to 2022. Cash used in activities decreased by 9% to EUR 10.1 mn. Cash and other current financial assets decreased to EUR 12.6 mn (31 December 2023).

NEWRON - FY 2023 RESULTS IN A NUTSHELL			
(IN EUR MN)	FY 2023	FY 2022	% CHANGE
REVENUES (LICENCE INCOME / ROYALTIES)	9.1	6.1	49%
- RESEARCH AND DEVELOPMENT EXPENSES	-13.2	-12.0	10%
- SALES, GENERAL AND ADMINISTRATIVE EXPENSES	-7.5	-7.4	2%
NET PROFIT / LOSS	-16.2	-17.5	-7%
CASH USED IN OPERATING ACTIVITIES	-10.1	-11.1	-9%
CASH & OTHER CURRENT FINANCIAL ASSETS (31 DECEMBER)	12.6	22.8	-45%

SOURCE: NEWRON PHARMACEUTICALS, VALUATIONLAB

Newron sufficiently funded into 2025 beyond key value inflection points

With EUR 12.6 mn in cash and short-term investments (31 December 2023), increasing royalty payments on Xadago sales, Italian R&D tax credits (approximately EUR 16mn in the next 2 years), the recent share subscription agreement with an institutional healthcare investor with up to EUR 15 mn in funding, and the deferral of the repayment of the first three tranches of the EUR 40 mn EIB loan by roughly 1 ½ years now starting in November 2025, Newron expects to be sufficiently funded well into 2025 beyond key value inflection points.

Following the unprecedented “Study 014/015” topline results, Newron is evaluating potential options for partnering or co-developing evenamide in schizophrenia to share the development risk, reduce the cash burn, and replenish its cash position. This will increase financial flexibility, which can be used to broaden the pipeline with promising external CNS compounds.

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 contracting new commercialization/distribution partners for Xadago beyond the EU, US, Japan, and Asia.
- Submit the exciting “Study 014/015” trial results to the FDA to address the remaining safety issues and finalize the protocol for the pivotal “Study 017” trial of evenamide in TRS.
- Report topline results of the first potentially pivotal phase II/III “Study 008A” trial of evenamide in schizophrenia in April 2024
- Start the second pivotal “Study 017” trial of evenamide in TRS patients in Q3 2024
- Determine potential options for global or local partnering or co-development and commercialization of evenamide before the start of the pivotal “Study 017”.
- Seek new CNS development projects to replenish the company’s development pipeline.

Valuation Overview

Sum-of-parts risk-adjusted (r)NPV points to a fair value of CHF 12.7 per share
We derive a sum-of-parts rNPV of CHF 12.7 per share, with cash of CHF 0.8 per share (31 December 2023), overhead of CHF 6.8 per share (including the repayment of the EUR 40 mn EIB loan starting in November 2025), with a WACC of 10% (consisting of a market risk premium of 6%, a beta of 1.5, and a risk-free rate (10-year Swiss bond yield) of 1%).

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	91	2015 (EU) I 2017 (US)	1.8	100%	1.8	9%
EVENAMIDE	SCHIZOPHRENIA (INADEQUATE RESPONDERS, TRS*)	903	2027	29.0	50%	14.5	74%
EVENAMIDE	CLOZAPINE TREATMENT-RESISTANT SCHIZOPHRENIA (CTRS)	137	2027	6.9	35%	2.4	12%
RALFINAMIDE	NEUROPATHIC PAIN	NON CORE					
CASH & CASH EQUIVALENTS (31 DECEMBER 2023)		13		0.8		0.8	4%
TOTAL ASSETS				**38.4**		**19.5**	**100%**
OVERHEAD EXPENSES (INCLUDING REPAYMENT OF THE EUR 40 MN EIB LOAN)				-6.8		-6.8	
NPV/SHARE (CHF)				**31.6**		**12.7**	
PRICE ON 25 MARCH 2024						7.5	
PERCENTAGE UPSIDE / (DOWNSIDE)						69%	

* TRS = TREATMENT RESISTANT SCHIZOPHRENIA

ESTIMATES AS OF 25 MARCH 2024

SOURCE: VALUATIONLAB ESTIMATES

Newron's key value drivers include:

Xadago (Parkinson's disease) - NPV of CHF 1.9 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. Following the agreement with generic manufacturers we now assume generic versions of Xadago to enter the US market as early as December 2027 (previously 2031). We assume Newron will receive from its partners Zambon (and sub-licensors) and Meiji Seika (and partner Eisai) royalties on sales ranging between 10-12% in EU/ROW, 7% in the US, and 2.5% in Japan. We calculate an NPV of CHF 1.9 per share with peak sales of around EUR 90 mn for Xadago in Parkinson's disease.

Evenamide (schizophrenia) – risk-adjusted NPV of CHF 14.5 per share
Evenamide targets a global USD 17 bn antipsychotics market. Evenamide could become the first add-on antipsychotic to be approved for inadequately responding and treatment-resistant schizophrenia (TRS) patients and the first drug for TRS since the approval of clozapine in 1989. Topline results of the first potentially pivotal phase II/III "Study 008A" trial of evenamide in non-TRS patients who inadequately respond to current antipsychotic monotherapy are expected in April 2024. The second pivotal "Study 017" phase III trial of evenamide in TRS is expected to start in Q3 2024, with topline results expected approximately 18 months later. Upon positive "Study 008A" results, we assume Newron to out-license the compound to a major CNS player for substantial upfront, regulatory, and sales milestone payments and royalties on sales. We forecast peak sales for evenamide to amount to around EUR 90 mn in schizophrenia and TRS (excluding CTRS), with the first launches in H1 2027. We calculate an rNPV of CHF 14.5 per share with a conservative 50% (single pivotal phase II/III) success rate, with Newron receiving up to EUR 387 mn in global upfront, development, regulatory, and sales milestones and 15% royalties on net sales.

Evenamide (CTRS) – risk-adjusted NPV of CHF 2.4 per share

Newron's development plans for evenamide to include clozapine treatment-resistant schizophrenia (CTRS) next to schizophrenia were triggered by the high unmet medical need for new treatments, with studies suggesting the involvement of the glutamate system in CTRS and US orphan disease designation. CTRS provides a fast-to-market indication (we expect the US launch in H1 2027 based on accelerated approval) with 7-year orphan disease market exclusivity upon US approval. We assume Newron to commercialize evenamide in CTRS in the US through a small in-house commercial team of key account managers and seek partners outside the US in return for EUR 15 mn upfront, development, regulatory, and sales milestones, and 15% royalties on net sales. We forecast peak sales to amount to EUR 137 mn. Our rNPV is CHF 2.4 per share with a conservative 35% (proof-of-concept established) success rate.

NOTE: Our success rate for evenamide in CTRS will increase to 50% (single potentially pivotal trial) when the second pivotal "Study 017" phase III trial of evenamide in TRS, including CTRS, starts in Q3 2024. Consequently, our rNPV for evenamide in CTRS will increase by CHF 1.0 per share to CHF 3.4 per share.

An additional upside to our forecasts could come from higher pricing 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. 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 evenamide as an add-on therapy for treating schizophrenia and CTRS. We have a conservative 50% (potentially pivotal phase II/III) success rate for evenamide in schizophrenia. Our 35% (POC established) success rate for CTRS will also increase to 50% once the phase III "Study 017" trial in TRS starts in Q3 2024. Successful development and approval of evenamide in schizophrenia will be transformational for Newron. The company has secured the necessary funds to develop evenamide in schizophrenia and CTRS. Additional funding is expected from the (global) partnering of evenamide.

Pricing and reimbursement: Following EMA and FDA approval, Xadago and evenamide must be priced and reimbursed by local healthcare providers. In the EU, pricing and reimbursement occur on a country-by-country base, leading to different pricing and reimbursement and potential market launch delays. Pricing and reimbursement have been established in the US.

Partnering: In 2012, Newron out-licensed Xadago to Zambon, which gained worldwide rights, excluding Japan and Asia, which Meiji Seika acquired. Zambon lacks a strong CNS presence in all markets and needs to secure strong commercialization partners in some regions. 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 global (co)development and commercialization partner for evenamide in schizophrenia in return for substantial upfront, development, regulatory and sales milestones, and royalties on sales. Partnering will reduce the development risk and cash burn and increase financial flexibility for Newron to acquire external CNS clinical compounds to boost its pipeline. Timing and terms could differ from our forecasts.

Commercialization: Newron's revenues and earnings for Xadago are entirely dependent on its commercialization partners to position successfully and market Xadago against existing Parkinson's treatments such as Teva's Azilect (rasagiline) and generic versions of rasagiline. Newron needs a major CNS player to commercialize evenamide in schizophrenia and other antipsychotic indications successfully. Revenues and earnings for evenamide in schizophrenia will depend entirely on its commercialization partner to successfully position and market evenamide against existing and new treatments. Newron plans to sell evenamide in CTRS in the US with a small in-house commercial team of key account managers, 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 rely heavily on the combination patent with levodopa that runs until 2024 (EU) and 2026 (US) with extensions of up to 5 years. A synthesis patent provides additional protection until 2027. We assume patent protection for Xadago in the EU/ROW until 2029 and following an agreement with several generic manufacturers who filed a Paragraph IV ANDA for Xadago in the US until December 2027. Evenamide's patent protection runs until 2028, with extensions of up to another five 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-year exclusivity in the EU.

Catalysts

CATALYST TIMELINES

TIME LINE	PRODUCT	INDICATION	MILESTONE	COMMENT	IMPACT ON RNPV/SHARE
2024					
4 JAN	EVENAMIDE	TREATMENT-RESISTANT SCHIZOPHRENIA (TRS)	"STUDY 014/15" - FINAL (1-YEAR) RESULTS	FINAL RESULTS OF THE 1-YEAR "STUDY 015" EXTENSION TRIAL OF EVENAMIDE AS ADD-ON TREATMENT TO ANTIPSYCHOTICS IN TRS SHOW UNPRECEDENTED RESULTS WITH >70% PATIENTS HAVING MEANINGFUL REDUCTION IN DISEASE SEVERITY, ~50% OF PATIENTS NO LONGER MEETING TRS PROTOCOL SEVERITY CRITERIA, AND ~25% ACHIEVING REMISSION (NEVER SEEN BEFORE IN A TRS TRIAL)	
14 MAR			SHARE SUBSCRIPTION AGREEMENT WITH INSTITUTIONAL INVESTOR	SHARE SUBSCRIPTION AGREEMENT WITH AND INSTITUTIONAL INVESTOR FOCUSED ON HIGH-GROWTH HEALTHCARE FIRMS; AN INITIAL 750,000 NEWLY ISSUED SHARES AT A SUBSCRIPTION PRICE OF EUR 7.33/SHARE WITH GROSS PROCEEDS OF EUR 5.5 MN; UP TO AN ADDITIONAL 1.3 MN NEWLY ISSUED SHARES UNTIL NO LATER THAN 31 JANUARY 2025 AT A SUBSCRIPTION PRICE ACCORDING TO AN AGREED FORMULA AMOUNTING UP TO EUR 9.5 MN IN ADDITIONAL PROCEEDS	
15 MAR			EIB AGREEMENT TO EXTEND EARLY TRANCHE REPAYMENT DATES	AGREEMENT WITH EIB (EUROPEAN INVESTMENT BANK) ON EUR 40 MN LOAN TO SHIFT REPAYMENT OF TRANCHES 1 (EUR 10 MN), 2 (EUR 7.5 MN) AND 3 (EUR 7.5 MN) FROM JUNE 2024 TO APRIL 2025 FOR NOVEMBER 2025, APRIL 2026 AND JUNE 2026 RESPECTIVELY; DUE DATES FOR TRANCHES 4 (EUR 7.5 MN) SEPTEMBER 2026 AND TRANCHE 5 (EUR 7.5 MN) OCTOBER 2026 REMAIN UNCHANGED ; THE EIB WILL QUALIFY FOR CERTAIN PERFORMANCE-BASED RENUMERATION	
19 MAR			FY 2023 RESULTS	CASH: EUR 12.6 MN (31 DECEMBER 2023) WITH CASH RUNWAY WELL INTO 2025 (INCLUDING ROYALTY INCOME & R&D TAX CREDIT, RECENT PROCEEDS RAISED UP TO EUR 15 MN); 2023 TOTAL REVENUES: EUR 9.1 MN (+49%) LARGELY FROM XADAGO ROYALTIES AND OTHER INCOME FROM CONTRACTS WITH CUSTOMERS	
APR	EVENAMIDE	NON-TREATMENT-RESISTANT RESISTANT SCHIZOPHRENIA (NTRS)	"STUDY 008A" - TOPLINE RESULTS (1ST PIVOTAL TRIAL)	TOPLINE RESULTS OF THE FIRST POTENTIALLY PIVOTAL PHASE II/III "STUDY 008A" OF EVENAMIDE AS AN ADD-ON THERAPY IN SCHIZOPHRENIA PATIENTS WHO ARE INADEQUATE RESPONDERS TO SECOND-GENERATION ANTIPSYCHOTICS; 4-WEEK, RANDOMIZED 30 MG BID EVENAMIDE VS. PLACEBO, DOUBLE-BLIND TRIAL IN >200 PATIENTS	
17 APR			AGM	APPOINTMENT OF MARGARITA CHAVEZ AS MEMBER OF THE BOARD; PROPOSAL TO INCREASE SHARE CAPITAL FOR A MAX OF 10% FOR 5-YEAR PERIOD; PROPOSAL TO INCREASE SHARE CAPITAL FOR A MAX OF 3% FOR OPTION PLAN(S) FOR 5-YEAR PERIOD	
BEFORE START "STUDY 017"	EVENAMIDE	SCHIZOPHRENIA	POTENTIAL PARTNERING AGREEMENT(S)	NEWRON EXPECTS A POTENTIAL (CO-) DEVELOPMENT AND COMMERCIALIZATION AGREEMENT(S) WITH (A) MAJOR CNS PLAYER(S) FOR EVENAMIDE TO ENHANCE DEVELOPMENT AND COMMERCIALIZATION, REDUCE CASH BURN AND STRENGTHEN ITS CASH POSITION	
Q3	EVENAMIDE	TREATMENT-RESISTANT SCHIZOPHRENIA (TRS)	START "STUDY 017" (2ND PIVOTAL TRIAL)	START SECOND POTENTIALLY PIVOTAL PHASE III "STUDY 017" OF EVENAMIDE IN TREATMENT-RESISTANT SCHIZOPHRENIA (TRS) INCLUDING CLOZAPINE TREATMENT-RESISTANT SCHIZOPHRENIA (CTRS) IN PATIENTS WITH ONE OF THE LEADING 2ND GENERATION ANTIPSYCHOTICS; 12-WEEK, RANDOMIZED, DOUBLE-BLIND PLACEBO-CONTROLLED GLOBAL TRIAL IN >510 TRS PATIENTS; TOPLINE RESULTS END 2025	+ CHF 1.0
19 SEP			H1 2024 RESULTS	H1 2024 RESULTS RELEASE; TYPICALLY NO CONFERENCE CALL	
DURING 2024			EXTERNAL CNS PIPELINE PRODUCTS	ONGOING SEARCH FOR STRATEGICALLY RELEVANT ASSETS TO ADD TO NEWRON'S CNS PIPELINE	

ESTIMATES AS OF 25 MARCH 2024 SOURCE: VALUATIONLAB ESTIMATES, NEWRON PHARMACEUTICALS

Key catalysts:

- **Results "Study 008A" of evenamide in non-TRS (April 2023):** the first, potentially pivotal, phase II/III trial of 30 mg evenamide twice-daily (BID) as add-on therapy in 291 schizophrenia patients who are inadequate responders to second-generation antipsychotics.
- **Partnering evenamide with a major CNS player (before starting "Study 017"**): Out-licensing evenamide to a major CNS player in return for substantial upfront, regulatory, and sales milestones and royalties on sales, extending the cash runway, which can be used to in-license new CNS compounds and sell evenamide in CTRS through a small in-house commercial team of key account managers in the US.
- **Start pivotal "Study 017" trial of evenamide in TRS (Q3 2024):** this marks the second potentially pivotal phase III trial needed for approval of evenamide in schizophrenia, including (clozapine) treatment-resistant schizophrenia; our success rate increases to 50% (phase II/III trial) from 35% (POC established) resulting in an increase of our rNPV by CHF 1.0 per share.

Technology & Pipeline

Search & Development company focused on CNS and orphan diseases
Newron has two drugs addressing multi-billion-dollar markets, including Xadago (Parkinson's disease), and evenamide (schizophrenia).

PRODUCT PIPELINE

PRODUCT	DRUG CLASS	INDICATION	STATUS	LAUNCH DATE (EXPECTED)	PARTNER	PEAK SALES
XADAGO	ALPHA-AMINOAMIDE	PARKINSON'S DISEASE	EU: LAUNCHED US: APPROVED	EU: H1 2015 US: JULY 2017	ZAMBON/MEIJI SEIKA/ EISAI/SUPERNUS PHARMA	EUR 90 MN
EVENAMIDE	ION CHANNEL BLOCKER	SCHIZOPHRENIA (MAJOR INDICATION)	PIVOTAL TRIAL "STUDY 008A" (RESULTS APRIL 2024)	H1 2027	PARTNER AFTER PIVOTAL TRIAL	EUR 900 MN
EVENAMIDE	ION CHANNEL BLOCKER	CLOZAPINE TREATMENT-RESISTANT SCHIZOPHRENIA (ORPHAN INDICATION)	PIVOTAL TRIAL "STUDY 017" (START Q3 2024)	H1 2027	PARTNER BEFORE 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 25 MARCH 2024
SOURCE: VALUATIONLAB ESTIMATES, NEWRON PHARMACEUTICALS

Xadago generates 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 rollout of Xadago is well on its way, with Xadago now available in 16 European countries with 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. Zambon and its regional partners have also 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. Partners Meiji Seika and Eisai received Japanese approval in September 2019, where the drug is branded Equfina.

Topline results of the first pivotal trial of evenamide in schizophrenia due April 2024
After the setback of sarizotan in Rett syndrome in May 2020, and with sufficient cash secured, Newron stepped up its development plans for evenamide in schizophrenia and CTRS. In September 2021, the pivotal development in non-TRS or patients who inadequately respond to current antipsychotic monotherapy started with the first potentially pivotal phase II/III “Study 008A” trial, with topline results expected to be reported in April 2024. The second potentially pivotal phase II/III trial, “Study 017” in TRS, including CTRS, is planned to start in Q3 2024, with topline results expected to be reported approximately 18 months later.

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

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

Strategy to complement CNS portfolio with rare disease opportunities
Newron also 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 of less than 1 per 2,000/5,000 people. Although orphan diseases may be classified individually as rare, they collectively 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 of orphan drugs include:
- A 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 the 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
- A relatively small salesforce can address specialists

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, as well as 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 of 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. 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 of Newron's key drivers, including:

- **Evenamide as an add-on therapy for schizophrenia/CTRS** (page 12)
- **Xadago in Parkinson's disease** (page 20)

Forecasts & Sensitivity Analysis

Evenamide (schizophrenia)

Product Analysis

Evenamide all schizophrenia indications: peak sales EUR 1 bn, rNPV CHF 16.9/share

1) Schizophrenia peak sales of EUR 900 mn - rNPV of CHF 14.5 per share

We forecast peak sales of EUR 903 mn for evenamide in its major indication as an add-on to existing schizophrenia therapy. Results of the first potentially pivotal "Study 008A" in non-TRS (schizophrenia patients who inadequately respond to current antipsychotic monotherapy) are expected to be reported in April 2024. A second potentially pivotal "Study 017" trial in TRS, including CTRS, is planned to start in Q3 2024, with topline results due approximately 18 months later. We assume Newron will contract a global CNS player to fully develop and commercialize evenamide in schizophrenia and potentially other CNS disorders such as mania or depression before the start of the pivotal "Study 017" trial. The first launches in schizophrenia are expected in H1 2027 with global patent protection until 2033 (including patent term extensions), 10-year data exclusivity on approval in the EU (2036), a conservative daily treatment cost of between USD 15 (US), and EUR 10 (EU/ROW), and a target market penetration peaking at ~14% (EU/ROW) and ~15% (US). Our rNPV amounts to CHF 258 mn, or CHF 14.5 per share, assuming Newron receives a total of EUR 387 mn of upfront and milestone payments, 15% royalties on sales, with a 50% (potentially pivotal phase II/III) success rate, and a WACC of 10% (see page 18).

2) CTRS peak sales of EUR 100+ mn – rNPV of CHF 2.4 per share

The orphan-like indication CTRS (clozapine treatment-resistant schizophrenia) is a niche indication with high unmet medical that Newron would like to market with a small in-house commercialization team in the US to optimize the long-term value. The potentially pivotal phase II/III "Study 017" trial of evenamide in TRS, including CTRS, is expected to start in Q3 2023 with topline results approximately 18 months later, with a potential US launch (assuming priority review) in H1 2027. We conservatively forecast peak sales to amount to EUR 137 mn, assuming the same pricing as for schizophrenia. We calculate an rNPV of CHF 43 mn or CHF 2.4 per share, assuming Newron commercializes evenamide in CTRS in the US and partners the drug in CTRS outside the US to the same partner(s) as for schizophrenia with a 15% royalty rate, EUR 15 mn global milestone payments, and a 15% (proof-of-concept established) success rate (see page 19).

NOTE: Our rNPV for CTRS will increase by CHF 1.0 per share to CHF 2.4 per share upon the start of "Study 017" in Q3 2024 with a 50% success rate. 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.

Evenamide is potentially the first add-on treatment for schizophrenia

Evenamide is potentially the first-ever add-on treatment for schizophrenia and the first treatment for treatment-resistant schizophrenia (TRS) since the launch of clozapine (branded Clozaril by Novartis) in 1989. Evenamide stems from Newron's ion channel discovery efforts and has shown benefit in various 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 high availability in the brain. Evenamide targets a large global antipsychotic market worth more than 17 bn despite being affected by several branded drugs losing patent protection. The schizophrenia market is worth approximately USD 7.5 bn, despite low patient compliance and many patients responding poorly to current antipsychotic therapy. Evenamide can be added to current antipsychotic therapy for patients who inadequately respond or have become treatment-resistant to current antipsychotic treatment (roughly 70% of patients). In 2017, Newron completed a phase IIa proof-of-concept (POC) trial of evenamide in schizophrenia (see Appendix, page 25). Evenamide enjoys an extensive patent life running until at least 2033 (including 5 5-year patent term extension), thanks to the US Patent and Trade Organization (USPTO) 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-year orphan drug market exclusivity upon approval in the US and EU, respectively. First launches in schizophrenia are expected to occur in the US in H1 2027, while we expect peak sales of evenamide to reach approximately EUR 1 bn for all schizophrenia indications.

Evenamide being developed in two indications covering roughly 70% of patients

It is estimated that only ~30% of schizophrenia patients respond well to monotherapy. Based on the positive POC results, evenamide is being developed as an add-on therapy to current antipsychotic medication for schizophrenia patients who 1) respond poorly to current antipsychotic monotherapy (~40% of schizophrenia patients), and 2) for treatment-resistant schizophrenia (TRS) patients (~30% of schizophrenia patients), including clozapine treatment-resistant schizophrenia (CTRS) patients, which is considered an orphan indication. In clinical practice, the delineation between inadequate responders and treatment-resistant schizophrenia patients becomes blurry. Patient treatment management is similar, which includes raising the monotherapy dose, switching monotherapy, treatment with multiple therapies, and depot injection for continuous treatment. Evenamide would become a first-in-class voltage-gated, selective sodium channel blocker specifically developed as a simple add-on to existing treatment regimens for schizophrenia and (C)TRS patients. Therefore, evenamide has the potential to be developed in fixed-dose combinations with existing treatments with the potential to extend their patent life substantially.

New drugs are desperately needed for TRS, which occurs in roughly 33% of patients

New therapeutic options are desperately needed for TRS, which occurs in approximately one-third of patients. The magnitude of the improvements experienced by these TRS patients, not responding to their current antipsychotic on evenamide, was substantial. The data comparing the impact of evenamide at six weeks versus six months suggest that not only was there sustained improvement in the key measures, but the proportion of patients achieving clinically meaningful improvement increased over time. If the planned randomized and placebo-controlled pivotal “Study 017” trial confirms these results, evenamide would be the first medication that could be added to an antipsychotic to improve symptoms in treatment-resistant schizophrenia and a breakthrough treatment in this difficult-to-treat patient group. This would support the hypothesis that evenamide treatment is associated with attenuating abnormal glutamate activity in TRS patients.

CTRS provides a fast-to-market route, 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 significant benefits, including:

- A fast-to-market opportunity (orphan indication with shorter development time, lower development costs, expedited review)
- 7-year (US) and 10-year (EU) orphan drug exclusivity from the date of approval
- Potential for parallel development of evenamide in schizophrenia
- Potential for Newron to market evenamide in CTRS through its own small specialist sales force in the lucrative US market 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 high morbidity (e.g., hospitalization) and mortality rate (e.g., suicide), with some of the highest hospitalization rates and costs to society, with an estimated USD 34 bn in direct healthcare costs in the US alone.

Roughly 30% of treatment-resistant schizophrenia patients fail clozapine treatment
Clozapine, a dopamine and serotonin antagonist (5HT2A) that was first introduced in the 1960s 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 in suicide attempts. Unfortunately, roughly 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 systems. A similar prevalence is estimated for the EU, Japan, and Canada.

Major regulators have agreed with Newron's evenamide phase III development plans
The health regulators in Spain, Denmark, Sweden, Germany, the UK, US, Canada, and the CHMP (the European Medicines Agency's Committee for Medicinal Products for Human Use) have agreed with Newron's proposed phase III development plan, which consists of two potentially pivotal phase II/III trials including:

1) **"Study 008A" in non-treatment-resistant schizophrenia (non-TRS) or inadequate responders** is an international, four-week, double-blind, placebo-controlled, potentially pivotal phase IIb/III trial designed to evaluate the efficacy, tolerability, and safety (including effects on electroencephalogram (EEC) of the 30 mg twice-daily (BID) dose of evenamide in chronic moderate to severe schizophrenia patients on second-generation antipsychotics. 291 patients were enrolled in several trial centers across Europe, Asia, and Latin America. Patients were randomized equally in two treatment arms, including 1) evenamide 30 mg BID plus a second-generation antipsychotic, and 2) placebo plus a second-generation antipsychotic, and treated for 4 weeks. The primary endpoint is the improvement in the PANSS Total Score from baseline. Secondary endpoints include

additional efficacy scores and safety and tolerability measures. The trial started in September 2021, with topline results expected to report in April 2024.

2) **"Study 017" in TRS (including the orphan indication CTRS)** is the first-ever, global, potentially pivotal phase II/III trial for a New Chemical Entity (NCE) as add-on therapy in TRS patients. The trial will enroll more than 510 adult TRS patients in a randomized, double-blind, placebo-controlled, 12-week, global trial to evaluate the efficacy and safety of two fixed doses (15 mg and 30 BID) of evenamide as an add-on treatment in TRS patients not responding to their current atypical antipsychotics (requiring a history of failure on two or more antipsychotics (two different chemical classes: at least one second-generation antipsychotic for an adequate period including a prospective failure)). The primary efficacy endpoint will be the PANNSS Total Score at the endpoint (Day 57 or endpoint). The key secondary efficacy endpoint is the change from baseline of the Clinical Global Impression Change (CGI-C). Safety and tolerability will be based on adverse events, adverse dropouts, serious adverse events, vital signs, laboratory evaluations, electrocardiogram (ECG), the Extrapyramidal Symptom Rating Scale-Abbreviated (ESRS-A), and the Calgary Depression Scale for Schizophrenia (CDSS), among others. "Study 017" is expected to start in Q3 2024, with topline results expected to be reported approximately 18 months later with an estimated cost of EUR ~40 mn.

The FDA delayed the start of the pivotal development due to safety concerns

Newron originally wanted to start the pivotal development of evenamide in schizophrenia and TRS in 2019. Unfortunately, in May 2019, the FDA signaled potential chronic toxicity concerns with evenamide in a study in rats and CNS (central nervous system) events at high doses in a study with dogs, with a 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 a 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 the absence of toxicity were already submitted to the FDA to support this data package. "Study 008" was designed to primarily assess safety and was not powered to demonstrate efficacy. The 7.5 mg twice daily (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 (Positive and Negative Symptom Score) than 7.5 mg BID. However, this was not statistically significant compared to placebo (see Appendix, page 27).

"Study 014/015" final FDA safety trial before starting the pivotal "Study 017" TRS trial

"Study 014" and its long-term, 1-year extension "Study 015" trial is the final safety requirement by the FDA before starting the pivotal phase III "Study 017" of evenamide in TRS, including clozapine treatment-resistant schizophrenia (CTRS). "Study 014" is an

international, randomized, open-label, rater-blinded trial of evenamide as an add-on to an antipsychotic (excluding clozapine) in patients with moderate to severe treatment-resistant schizophrenia who were no longer responding to their current antipsychotic medication.

The primary objective of "Study 014" is to evaluate the safety and tolerability of evenamide in three oral fixed doses of 7.5 mg, 15 mg, and 30 mg twice daily (BID) for 6 weeks in 161 patients with TRS. The secondary objective is the assessment of preliminary efficacy that includes the changes from baseline in the Positive and Negative Syndrome Scale (PANSS) total score, Clinical Global Impression of Change (CGI-C) and Severity of Illness (CGI-S), Strauss-Carpenter Level of Functioning (LOF), and Medication Satisfaction Questionnaire (MSQ), among others. "Study 015" is the 1-year extension arm of the trial.

Compelling topline results of "Study 014" with safety & efficacy in line with previous interim results first 100 patients

In March 2023, compelling topline results from the "Study 014" trial in 161 patients with moderate to severe treatment-resistant schizophrenia (TRS) not responding to their current antipsychotic medication showed a statistically significant improvement over baseline in all efficacy measures at the 6-week primary endpoint (see Appendix, page 28)

"Study 015" 1-year results show unprecedented efficacy, with ~25% of TRS patients in remission (cure) and >70% experiencing a meaningful reduction in disease severity

On 4 January 2024, Newron reported unprecedented efficacy results of the open-label (unblinded) "Study 015" 1-year extension trial of the 6-week phase II "Study 014" safety and dose-ranging trial of evenamide as an add-on to current antipsychotics in treatment-resistant schizophrenia (TRS) patients. Evenamide was safe and well-tolerated at one-year treatment in TRS patients, with >70% of patients experiencing a clinically meaningful reduction in disease severity, ~50% of patients no longer meeting any of the TRS protocol severity criteria, and ~25% of patients achieving remission (cure), which has never been seen before in this treatment population. Moreover, the clinically significant benefit of evenamide was sustained and increased throughout the one-year treatment course. The increasing benefit over time from six weeks to one year suggests that the glutamate-modulating effect of evenamide could lead to a progressive and long-standing alteration in brain processes synergizing with the effect of antipsychotics to which the patient had become resistant with the potential to transform the management and societal outlook for these difficult to treat TRS patients (see Appendix, page 30).

Newron expected to contract a (global) partner for evenamide on the exciting news

Newron is evaluating potential options for partnering or co-developing the further development of evenamide in schizophrenia and other related indications such as mania or depression. Based on the exciting "Study 014/015" interim data, we assume Newron to sign a global or local (co)development and commercialization agreement with a major CNS player in return for substantial upfront, regulatory, and commercial milestones and royalties on sales before the start of the pivotal trial "Study 017" in Q3 2024. Partnering would strengthen the company's cash position to in-license external CNS and rare disease clinical compounds. We assume Newron will sell evenamide in the CTRS orphan indication in the lucrative US market by a small in-house commercialization team of key account managers to optimize its long-term value.

Evenamide has a global peak sales potential of EUR 1 bn

To correctly reflect and value Newron's plans to develop evenamide in two indications, the major being schizophrenia (inadequate responders and treatment-resistant schizophrenia) and the orphan indication CTRS, we have made separate forecasts for each indication.

1) Schizophrenia (major indication) peak sales potential of EUR 900 mn

Worldwide, more than 21 mn people are suffering from schizophrenia, of which more than 2 mn are in the US and around 5 mn in the EU, Japan, and Australia. Roughly 70% of schizophrenia patients experience positive symptoms and are treated with typical and atypical antipsychotics, of which only 25% of patients are 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 a substantial upside to our forecasts in schizophrenia. In 2024, we expect Newron will out-license evenamide to a strong global CNS player in return for substantial upfront, development, regulatory, and sales milestone payments and 15% royalties on net sales. The first launches are expected in H1 2027.

In our detailed evenamide (see page 18) forecasts, we have accounted for two major regions, namely:

1) **Europe/ROW:** We forecast peak sales of EUR 612 mn, assuming a conservative daily treatment price of EUR 10, 10 years of data exclusivity, and a peak penetration rate of ~14%. We assume milestone payments of EUR 245 mn.
2) **US:** Peak sales of EUR 403 mn, assuming a conservative daily treatment price of USD 15, patent protection until 2033 (including a 5-year patent term extension), and a peak penetration rate of ~15%. We assume milestone payments of EUR 145 mn.

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

Of the TRS patients, approximately 12% are treated with clozapine, which is the target population for evenamide, which will be used as an add-on to clozapine. We expect high peak market penetration rates due to the severity of the illness and the 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. The first launches are expected in 2025. We assume Newron will sell evenamide in CTRS in the US through its small in-house commercialization team. Outside the US, we expect Newron to out-license the CTRS rights to the same commercialization partners (see page 19).

1) **Europe/ROW:** We forecast peak sales of EUR 64 mn, assuming a conservative daily treatment price of EUR 10, 10 years of orphan drug exclusivity, and a peak penetration rate of ~35%. We assume total milestone payments of EUR 15 mn.
2) **US:** Peak sales of EUR 79 mn, assuming a conservative daily treatment price of USD 15, patent protection until 2033 (including a 5-year patent term extension), and a peak penetration rate of ~60%. We account for the buildup of a small specialist sales force and assume COGS to amount to 15% of sales.

NOTE: Evenamide's potential could be substantially larger than our forecasts based on conservative pricing assumptions, the size of the market, and additional indications such as depression or mania.

Forecasts & Sensitivity Analysis

Schizophrenia - Inadequate responders (non-TRS) and TRS (excl. CTRS)

EVENAMIDE - FINANCIAL FORECASTS FOR SCHIZOPHRENIA

INDICATION	ADD-ON THERAPY TO ANTIPSYCHOTICS FOR REDUCING POSITIVE SYPMTOMS AND PSYCHOTIC WORSENING IN PATIENTS WITH SCHIZOPHRENIA
DOSAGE	30 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 ANTIPSYCHOTICS 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	PHASE II/III "STUDY 008A" (NON-TRS) RESULTS APRIL 2024; PHASE III "STUDY 017" (TRS) START Q3 2024, RESULTS END 2025, LAUNCH H1 2027
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 REGISTRATIONAL TRIALS; GLOBAL PARTNERING LIKELY ON POSITIVE "STUDY 008A" RESULTS

REVENUE MODEL

EUROPE / REST OF WORLD (PARTNER TBD)	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**	**2033E**
NUMBER OF PATIENTS (MN)	5.7	5.8	5.9	6.0	6.1	6.2	6.3	6.4	6.5	6.5	6.6
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)	4.0	4.1	4.1	4.2	4.3	4.3	4.4	4.4	4.5	4.6	4.7
COMPLIANCE RATE (%)	25%	25%	25%	25%	25%	25%	25%	25%	25%	25%	25%
PATIENTS TREATED	1,002,020	1,017,051	1,032,306	1,047,791	1,063,508	1,079,460	1,095,652	1,112,087	1,128,768	1,145,700	1,162,886
-/- PATIENTS WITH CTRS (SEE EVANAMIDE CTRS MODEL)	-42,211	-42,844	-43,487	-44,139	-44,801	-45,473	-46,155	-46,848	-47,550	48,264	48,988
INADEQUATE RESPONDERS (~57%)	547,091	555,298	563,627	572,082	580,663	589,373	598,213	607,186	616,294	625,539	634,922
TREATMENT RESISTANT SCHIZOPHRENIA (TRS) PATIENTS (~43%)	412,718	418,909	425,192	431,570	438,044	444,614	451,284	458,053	464,924	471,898	478,976
PATIENTS TREATED (EXCLUDING CTRS PATIENTS)	959,809	974,206	988,820	1,003,652	1,018,707	1,033,987	1,049,497	1,065,239	1,081,218	1,097,436	1,113,898
PENETRATION (%)	0%	0%	0%	0%	5%	8%	10%	11%	12%	13%	13%
NUMBER OF TREATED PATIENTS	0	0	0	0	50,935	82,719	104,950	117,176	129,746	137,180	144,807
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**	**186**	**302**	**383**	**428**	**474**	**501**	**529**
CHANGE (%)						62%	27%	12%	11%	6%	6%
ROYALTY (%)	15%	15%	15%	15%	15%	15%	15%	15%	15%	15%	15%
ROYALTIES (EUR MN)	0	0	0	0	28	45	57	64	71	75	79
UPFRONT & MILESTONE PAYMENTS (EUR MN)		20	10	20	15	30		40		50	
R&D COSTS	-12	-2	0	0	0	0	0	0	0	0	0
PROFIT BEFORE TAX (EUR MN)	**-12**	**18**	**10**	**20**	**43**	**75**	**57**	**104**	**71**	**125**	**79**
TAXES (EUR MN)	0	-1	-2	-3	-13	-24	-18	-33	-22	-39	-25
PROFIT (EUR MN)	**-12**	**17**	**8**	**17**	**29**	**52**	**39**	**71**	**49**	**86**	**54**

UNITED STATES (PARTNER TBD)	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**	**2033E**
NUMBER OF PATIENTS (MN)	2.7	2.7	2.8	2.8	2.8	2.9	2.9	3.0	3.0	3.1	3.1
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)	1.9	1.9	1.9	2.0	2.0	2.0	2.0	2.1	2.1	2.1	2.2
COMPLIANCE RATE (%)	25%	25%	25%	25%	25%	25%	25%	25%	25%	25%	25%
PATIENTS TREATED	467,218	474,226	481,339	488,559	495,888	503,326	510,876	518,539	526,317	534,212	542,225
-/- PATIENTS WITH CTRS (SEE EVENAMIDE CTRS MODEL)	-22,962	-23,307	-23,656	-24,011	-24,371	-24,737	-25,108	-25,485	-25,867	26,255	26,649
INADEQUATE RESPONDERS (~57%)	253,226	257,024	260,879	264,793	268,764	272,796	276,888	281,041	285,257	289,536	293,879
TREATMENT RESISTANT SCHIZOPHRENIA (TRS) PATIENTS (~43%)	191,030	193,895	196,804	199,756	202,752	205,793	208,880	212,013	215,194	218,422	221,698
PATIENTS TREATED (EXCLUDING CTRS PATIENTS)	444,255	450,919	457,683	464,548	471,516	478,589	485,768	493,055	500,450	507,957	515,577
PENETRATION (%)	0%	0%	0%	0%	6%	10%	12%	13%	14%	15%	8%
NUMBER OF TREATED PATIENTS	0	0	0	0	29,753	50,333	61,305	67,410	73,684	80,132	40,667
COST OF THERAPY PER YEAR (EUR)	5,113	5,026	5,026	5,026	5,026	5,026	5,026	5,026	5,026	5,026	5,026
SALES (EUR MN)	**0**	**0**	**0**	**0**	**150**	**253**	**308**	**339**	**370**	**403**	**204**
CHANGE (%)						69%	22%	10%	9%	9%	-49%
ROYALTY (%)	15%	15%	15%	15%	15%	15%	15%	15%	15%	15%	15%
ROYALTIES (EUR MN)	0	0	0	0	22	38	46	51	56	60	31
UPFRONT & MILESTONE PAYMENTS (EUR MN)	0	18	0	18	18	23	28	0	37	0	0
PROFIT BEFORE TAX (USD MN)	**0**	**20**	**0**	**20**	**44**	**66**	**80**	**55**	**101**	**66**	**33**
TAXES (EUR MN)	0	-1	0	-3	-13	-19	-23	-16	-29	-19	-10
PROFIT (EUR MN)	**0**	**17**	**0**	**15**	**28**	**42**	**51**	**35**	**63**	**41**	**21**

	2023E	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**	**2033E**
GLOBAL SALES (EUR MN)	**0**	**0**	**0**	**0**	**335**	**555**	**691**	**766**	**844**	**903**	**733**
CHANGE (%)						65%	25%	11%	10%	7%	-19%
GLOBAL PROFIT (EUR MN)	**-12**	**35**	**8**	**32**	**57**	**93**	**90**	**106**	**112**	**127**	**75**
CHANGE (%)	2%	-388%	-77%	298%	78%	63%	-4%	18%	5%	14%	-41%

WACC (%)	10%	
NPV TOTAL PROFIT (CHF MN)	**517**	
NUMBER OF SHARES (MN)	17.8	
NPV PER SHARE (CHF)	29	
SUCCESS PROBABILITY	50%	(SINGLE POTENTIALLY PIVOTAL PHASE IIB TRIAL)
RISK ADJUSTED NPV PER SHARE (CHF)	**14.5**	

SENSITIVITY ANALYSIS

		WACC (%)				
	CHF/SHARE	8	9	10	11	12
	100%	32.8	30.8	29.0	27.3	25.7
	90%	29.5	27.7	26.1	24.5	23.1
	80%	26.3	24.6	23.2	21.8	20.6
SUCCESS PROBABILITY	70%	23.0	21.6	20.3	19.1	18.0
	60%	19.7	18.5	17.4	16.4	15.4
	50%	16.4	15.4	**14.5**	13.6	12.9
	40%	13.1	12.3	11.6	10.9	10.3

ESTIMATES AS OF 25 MARCH 2024

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 OR 30 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-YEAR DATA EXCLUSIVITY
PHASE	FILINGS RELATING TO ORPHAN/PRIME/FAST TRACT DESIGNATION; START PHASE III "STUDY 017" TRS TRIAL Q3 2024, RESULTS END 2025; LAUNCH H1 2027
PATHWAY	PHASE III TRIAL IN INADEQUATE RESPONDERS + PHASE III TRIAL IN TREATMENT-RESISTANT SCHIZOPHRENIA (INCL. CTRS); 18 MONTHS TO COMPLETION FOR EACH TRIAL
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)	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**	**2033E**
NUMBER OF PATIENTS (MN)	5.7	5.8	5.9	6.0	6.1	6.2	6.3	6.4	6.5	6.5	6.6
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)	4.0	4.1	4.1	4.2	4.3	4.3	4.4	4.4	4.5	4.6	4.7
TREATMENT-RESISTANT SCHIZOPHRENIA (%)	30%	30%	30%	30%	30%	30%	30%	30%	30%	30%	30%
TREATMENT-RESISTANT SCHIZOPHRENIA PATIENTS	1,202,424	1,220,461	1,238,768	1,257,349	1,276,209	1,295,353	1,314,783	1,334,505	1,354,522	1,374,840	1,395,463
PATIENTS ON CLOZAPINE (%)	12%	12%	12%	12%	12%	12%	12%	12%	12%	12%	12%
PATIENTS ON CLOZAPINE	140,703	142,814	144,956	147,131	149,338	151,578	153,851	156,159	158,501	160,879	163,292
CLOZAPINE-RESISTANT SCHIZOPHRENIA (%)	30%	30%	30%	30%	30%	30%	30%	30%	30%	30%	30%
CLOZAPINE-RESISTANT SCHIZOPHRENIA PATIENTS	42,211	42,844	43,487	44,139	44,801	45,473	46,155	46,848	47,550	48,264	48,988
PENETRATION (%)	0%	0%	0%	0%	12%	20%	26%	30%	32%	33%	34%
NUMBER OF TREATED PATIENTS	0	0	0	0	5,376	9,095	12,000	14,054	15,216	15,927	16,656
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**	**20**	**33**	**44**	**51**	**56**	**58**	**61**
CHANGE (%)						69%	32%	17%	8%	5%	5%
ROYALTY (%)	15%	15%	15%	15%	15%	15%	15%	15%	15%	15%	15%
ROYALTIES (EUR MN)	0	0	0	0	3	5	7	8	8	9	9
UPFRONT & MILESTONE PAYMENTS (EUR MN)		5		5				5			
R&D COSTS	-1	-2	-2	0	0	0	0	0	0	0	0
PROFIT BEFORE TAX (EUR MN)	**-1**	**3**	**-2**	**5**	**3**	**5**	**7**	**13**	**8**	**9**	**9**
TAXES (EUR MN)	0	0	0	-1	-1	-2	-2	-4	-3	-3	-3
PROFIT (EUR MN)	**-1**	**3**	**-2**	**4**	**2**	**3**	**5**	**9**	**6**	**6**	**6**

UNITED STATES (NEWRON SPECIALIST SALES FORCE)	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**	**2033E**
NUMBER OF PATIENTS (MN)	2.7	2.7	2.8	2.8	2.8	2.9	2.9	3.0	3.0	3.1	3.1
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)	1.9	1.9	1.9	2.0	2.0	2.0	2.0	2.1	2.1	2.1	2.2
TREATMENT-RESISTANT (%)	35%	35%	35%	35%	35%	35%	35%	35%	35%	35%	35%
TREATMENT-RESISTANT SCHIZOPHRENIA	654,105	663,916	673,875	683,983	694,243	704,657	715,226	725,955	736,844	747,897	759,115
PATIENTS ON CLOZAPINE (%)	12%	12%	12%	12%	12%	12%	12%	12%	12%	12%	12%
PATIENTS ON CLOZAPINE	76,541	77,689	78,854	80,037	81,238	82,456	83,693	84,949	86,223	87,516	88,829
CLOZAPINE-RESISTANT SCHIZOPHRENIA (%)	30%	30%	30%	30%	30%	30%	30%	30%	30%	30%	30%
CLOZAPINE-RESISTANT SCHIZOPRENIA PATIENTS	22,962	23,307	23,656	24,011	24,371	24,737	25,108	25,485	25,867	26,255	26,649
PENETRATION (%)	0%	0%	0%	0%	20%	32%	42%	50%	56%	60%	18%
NUMBER OF TREATED PATIENTS	0	0	0	0	4,874	7,916	10,545	12,742	14,485	15,753	4,797
COST OF THERAPY PER YEAR (EUR)	5,113	5,026	5,026	5,026	5,026	5,026	5,026	5,026	5,026	5,026	5,026
SALES (EUR MN) - BOOKED BY NEWRON	**0**	**0**	**0**	**0**	**24**	**40**	**53**	**64**	**73**	**79**	**24**
CHANGE (%)						62%	33%	21%	14%	9%	-70%
COGS (%)	15%	15%	15%	15%	15%	15%	15%	15%	15%	15%	15%
COGS (EUR MN)	0	0	0	0	-4	-6	-8	-10	-11	-12	-4
S,G&A (EUR MN)	0	0	0	0	-7	-8	-9	-11	-12	-13	-4
PROFIT BEFORE TAX (EUR MN)	**0**	**0**	**0**	**0**	**14**	**26**	**36**	**44**	**50**	**54**	**16**
TAXES (EUR MN)	0	0	0	0	-4	-8	-11	-14	-16	-17	-5
PROFIT (EUR MN)	**0**	**0**	**0**	**0**	**10**	**18**	**25**	**30**	**34**	**37**	**11**

	2023E	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**	**2033E**
GLOBAL SALES (EUR MN)	**0**	**0**	**0**	**0**	**44**	**73**	**97**	**115**	**128**	**137**	**85**
CHANGE (%)						65%	33%	19%	11%	7%	-38%
GLOBAL PROFIT (EUR MN)	**-1**	**3**	**-2**	**4**	**12**	**21**	**29**	**39**	**40**	**43**	**18**
CHANGE (%)	476%	-347%	-157%	-360%	179%	80%	38%	32%	3%	8%	-59%
WACC (%)	10%										
NPV TOTAL PROFIT (CHF MN)	**122**										
NUMBER OF SHARES (MN)	17.8										
NPV PER SHARE (CHF)	7										
SUCCESS PROBABILITY	35%	(PROOF-OF-CONCEPT ESTABLISHED)									
RISK ADJUSTED NPV PER SHARE (CHF)	**2.4**										

SENSITIVITY ANALYSIS

		WACC (%)				
	CHF/SHARE	8	9	10	11	12
	100%	7.8	7.3	6.9	6.4	6.1
	80%	6.2	5.8	5.5	5.2	4.8
	65%	5.1	4.8	4.5	4.2	3.9
SUCCESS PROBABILITY	50%	3.9	3.7	3.4	3.2	3.0
	35%	2.7	2.6	**2.4**	2.3	2.1
	25%	1.9	1.8	1.7	1.6	1.5
	15%	1.2	1.1	1.0	1.0	0.9

ESTIMATES AS OF 25 MARCH 2024

SOURCE: VALUATIONLAB ESTIMATES

Xadago (Parkinson's disease)

Product Analysis

Parkinson's peak sales of EUR 90 mn - rNPV of CHF 1.9 per share

We forecast peak sales of EUR 91 mn for Xadago in its major indication of Parkinson's disease. Xadago was launched in the EU in 2015, followed by the US in 2017 and Japan in 2019. We assume EU patent protection until 2029, no generic versions of Xadago in the US until December 2027 (following an agreement with generic manufacturers in the US), a daily treatment cost of USD 9 (US), EUR 2.80 (EU/ROW), and EUR 4 (Japan/Asia), and a market penetration peaking between ~1-3%, hampered by cheap generic versions of Teva's Azilect (rasagiline). Our NPV amounts to CHF 33 mn, or CHF 1.9 per share, assuming royalties on sales ranging between 2.5% (Japan), 7% (US), and 10-14% (EU/ROW), with a WACC of 10% (for details, see following page).

US sales hampered by generic versions of Azilect

Xadago is Newron's first-ever launched product stemming from its ion channel research and was launched in the EU in 2015, in the US in 2017, and in Japan in 2019 (branded "Equfina") 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). In 2012, Xadago was licensed to Meiji Seika (Japan & Asian markets) and Zambon (worldwide excluding Meiji Seika markets). These partners and their sublicensees commercialize Xadago, including Supernus Pharma in the US, Medison Parma in Israel, Valeo in Canada (branded "Onstryv"), and Seqirus in Australia and New Zealand (see Appendix, page 24). Xadago is the first NCE (new chemical entity) approved in over a decade for treating Parkinson's disease. Xadago product sales have been trailing expectations, particularly in the US, due to the availability of cheap generic versions of Teva's Azilect (rasagiline), a competing MAO-B inhibitor. In 2021, several generic manufacturers filed so-called Paragraph IV ANDA Notice Letters for Xadago in the US to acquire "first-to-file" rights to sell their generic version of Xadago. Newron and its partners Zambon and Supernus have reached a settlement agreement with the generic manufacturers, allowing them to enter the US market no earlier than 1 December 2027. Supplementary Protection Certificates (SPCs) have been approved in most major markets, and the company is confident these will be granted in all key territories, protecting until 2029.

Parkinson's disease peak sales of around EUR 90 mn

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 67 mn, assuming a daily treatment price of EUR 2.80 and a peak penetration rate of ~3%. We also assume a tiered royalty rate increasing from 10% to 14%.
2) **US (Supernus Pharma):** Peak sales of EUR 23 mn with a daily treatment price of USD 9, a peak penetration of ~1%, and royalties on sales of ~7% with generics entering the US market in December 2027 from previously 2031.
3) **Japan/Asia (Meiji Seika & Eisai):** We forecast peak sales of EUR 7 mn and royalties on sales of ~2.5%.

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 AGREEMENT US GENERICS END 2027
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)	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**	**2033E**
NUMBER OF PATIENTS (MN)	4.0	4.1	4.2	4.3	4.3	4.4	4.5	4.6	4.7	4.8	4.9
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	2,807,126	2,863,269	2,920,534	2,978,945	3,038,524	3,099,294	3,161,280	3,224,506	3,288,996	3,354,776	3,421,871
-/- PATIENTS WITH PD-LID	538,968	549,748	560,743	571,957	583,397	595,065	606,966	619,105	631,487	644,117	0
PATIENTS TREATED WITHOUT PD-LID	2,268,158	2,313,521	2,359,792	2,406,988	2,455,127	2,504,230	2,554,314	2,605,401	2,657,509	2,710,659	3,421,871
PENETRATION (%)	2.1%	2.2%	2.3%	2.4%	2.5%	2.6%	2.1%	1.0%	0.5%	0.3%	0.1%
NUMBER OF TREATED PATIENTS	47,790	51,059	54,440	57,936	61,550	65,285	53,273	27,169	13,856	7,067	4,460
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)	**49**	**52**	**56**	**59**	**63**	**67**	**54**	**28**	**14**	**7**	**5**
CHANGE (%)	0%	7%	7%	6%	6%	6%	-18%	-49%	-49%	-49%	-37%
ROYALTY (%)	12%	12%	12%	12%	12%	12%	12%	12%	12%	12%	12%
ROYALTIES (EUR MN)	6	6	7	7	8	8	7	3	2	1	1
UPFRONT & MILESTONE PAYMENTS (EUR MN)											
PROFIT BEFORE TAX (EUR MN)	**6**	**6**	**7**	**7**	**8**	**8**	**7**	**3**	**2**	**1**	**1**
TAXES (EUR MN)	0	0	-1	-1	-2	-3	-2	-1	-1	0	0
PROFIT (EUR MN)	**6**	**6**	**5**	**6**	**5**	**5**	**4**	**2**	**1**	**1**	**0**

UNITED STATES (ZAMBON PARTNER SUPERNUS PHARMA)	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**	**2033E**
NUMBER OF PATIENTS (MN)	1.3	1.3	1.3	1.4	1.4	1.4	1.5	1.5	1.5	1.5	1.6
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	1,034,885	1,055,583	1,076,695	1,098,229	1,120,193	1,142,597	1,165,449	1,188,758	1,212,533	1,236,784	1,261,519
-/- PATIENTS WITH PD-LID	198,698	202,672	206,725	210,860	215,077	219,379	223,766	228,242	232,806	237,462	0
PATIENTS TREATED WITHOUT PD-LID	836,187	852,911	869,969	887,369	905,116	923,218	941,683	960,516	979,727	999,321	1,261,519
PENETRATION (%)	0.4%	0.5%	0.6%	0.7%	0.8%	0.2%	0.0%	0.0%	0.0%	0.0%	0.0%
NUMBER OF TREATED PATIENTS	3,600	4,525	5,485	6,482	7,517	1,533	313	64	13	3	1
COST OF THERAPY PER YEAR (EUR)	3,068	3,015	3,015	3,015	3,015	3,015	3,015	3,015	3,015	3,015	3,015
SALES (EUR MN)	**11**	**14**	**17**	**20**	**23**	**5**	**1**	**0**	**0**	**0**	**0**
CHANGE (%)	-16%	24%	21%	18%	16%	-80%	-80%	-80%	-80%	-80%	-75%
ROYALTY (%)	7%	7%	7%	7%	7%	7%	7%	7%	7%	7%	107%
ROYALTIES (EUR MN)	1	1	1	1	2	0	0	0	0	0	0
UPFRONT & MILESTONE PAYMENTS (EUR MN)	0	0	0	0	0	0	3	0	0	0	0
PROFIT BEFORE TAX (EUR MN)	**1**	**1**	**1**	**1**	**2**	**0**	**3**	**0**	**0**	**0**	**0**
TAXES (EUR MN)	0	0	0	0	0	0	-1	0	0	0	0
PROFIT (EUR MN)	**1**	**1**	**1**	**1**	**1**	**0**	**2**	**0**	**0**	**0**	**0**

JAPAN & ASIA PACIFIC (MEIJI SEIKA PARTNER EISAI)	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**	**2033E**
NUMBER OF PATIENTS	317,917	324,275	330,761	337,376	344,123	351,006	358,026	365,186	372,490	379,940	387,539
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	254,333	259,420	264,608	269,901	275,299	280,805	286,421	292,149	297,992	303,952	310,031
-/- PATIENTS WITH PD-LID	48,832	49,809	50,805	51,821	52,857	53,914	54,993	56,093	57,214	58,359	0
PATIENTS TREATED WITHOUT PD-LID	205,501	209,611	213,804	218,080	222,441	226,890	231,428	236,057	240,778	245,593	310,031
PENETRATION (%)	1.4%	1.4%	1.5%	1.6%	1.7%	1.8%	1.9%	2.0%	1.0%	0.5%	0.3%
NUMBER OF TREATED PATIENTS	2,774	2,935	3,207	3,489	3,782	4,084	4,397	4,721	2,408	1,228	775
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)	**4**	**4**	**5**	**5**	**6**	**6**	**6**	**7**	**4**	**2**	**1**
CHANGE (%)	6%	6%	9%	9%	8%	8%	8%	7%	-49%	-49%	-37%
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	0.1	0.1	0.1	0.2	0.2	0.1	0.0	0.0
UPFRONT & MILESTONE PAYMENTS (EUR MN)											
PROFIT BEFORE TAX (EUR MN)	**0.1**	**0.1**	**0.1**	**0.1**	**0.1**	**0.1**	**0.2**	**0.2**	**0.1**	**0.0**	**0.0**
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**	**0.1**	**0.1**	**0.1**	**0.1**	**0.1**	**0.0**	**0.0**

	2023E	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**	**2033E**
GLOBAL SALES (EUR MN)	**64**	**70**	**77**	**84**	**91**	**77**	**62**	**35**	**18**	**9**	**6**
CHANGE (%)	-3%	10%	10%	9%	9%	-15%	-20%	-44%	-49%	-49%	-37%
GLOBAL PROFIT (EUR MN)	**7**	**7**	**6**	**7**	**6**	**6**	**7**	**2**	**1**	**1**	**0**
CHANGE (%)	13%	3%	-7%	12%	-12%	-9%	12%	-63%	-49%	-49%	-37%
WACC (%)	10%										
NPV TOTAL PROFIT (CHF MN)	**34**										
NUMBER OF SHARES (MN)	17.8										
NPV PER SHARE (CHF)	**1.9**										

SENSITIVITY ANALYSIS

		WACC (%)				
	CHF/SHARE	8	9	10	11	12
	120	2.7	2.6	2.5	2.5	2.4
	110	2.5	2.4	2.3	2.3	2.2
	100	2.2	2.2	2.1	2.0	2.0
PEAK SALES	90	2.0	2.0	**1.9**	1.8	1.8
	80	1.8	1.7	1.7	1.6	1.6
	70	1.6	1.5	1.5	1.4	1.4
	60	1.3	1.3	1.3	1.2	1.2

ESTIMATES AS OF 25 MARCH 2024

SOURCE: VALUATIONLAB ESTIMATES

Income Statement

NEWRON PHARMACEUTICALS									SHARE PRICE (CHF)		7.50
IFRS											
INCOME STATEMENT (EUR MN)	2023	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E	2033E
PRODUCT SALES (INCLUDING PARTNERS)	**64**	**70**	**77**	**84**	**471**	**705**	**850**	**917**	**990**	**1,050**	**824**
CHANGE (%)	-3%	10%	10%	9%	461%	50%	21%	8%	8%	6%	-22%
PRODUCT SALES (BY NEWRON)	**0**	**0**	**0**	**0**	**24**	**40**	**53**	**64**	**73**	**79**	**24**
CHANGE (%)						62%	33%	21%	14%	9%	-70%
ROYALTIES	**7**	**7**	**8**	**9**	**63**	**97**	**117**	**126**	**137**	**145**	**120**
CHANGE (%)	13%	9%	9%	8%	627%	55%	21%	8%	8%	6%	-18%
LICENCE, UPFRONT & MILESTONE INCOME	**0**	**43**	**10**	**43**	**33**	**53**	**28**	**45**	**37**	**50**	**0**
OTHER INCOME & GRANTS	**2**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
REVENUES (EXCL. PARTNER SALES)	**9**	**51**	**18**	**52**	**120**	**190**	**198**	**235**	**246**	**274**	**144**
CHANGE (%)	49%	461%	-64%	188%	131%	57%	4%	19%	5%	11%	-48%
COGS	**0**	**0**	**0**	**0**	**-4**	**-6**	**-8**	**-10**	**-11**	**-12**	**-4**
GROSS PROFIT	**9**	**51**	**18**	**52**	**117**	**184**	**190**	**226**	**235**	**263**	**140**
CHANGE (%)	49%	461%	-64%	188%	124%	57%	3%	19%	4%	12%	-47%
MARGIN	100%	100%	100%	100%	97%	97%	96%	96%	96%	96%	97%
R&D	**-13**	**-10**	**-8**	**-8**	**-8**	**-9**	**-9**	**-10**	**-10**	**-11**	**-11**
CHANGE (%)	10%	-24%	-20%	0%	5%	5%	5%	5%	5%	5%	5%
S,G&A	**-8**	**-8**	**-8**	**-8**	**-14**	**-15**	**-17**	**-18**	**-20**	**-21**	**-12**
CHANGE (%)	2%	0%	0%	0%	88%	9%	7%	11%	8%	5%	-45%
OPERATING EXPENSES	**-21**	**-18**	**-16**	**-16**	**-26**	**-30**	**-34**	**-38**	**-41**	**-44**	**-27**
CHANGE (%)	7%	-15%	-11%	0%	69%	15%	11%	12%	9%	6%	-39%
AS % REVENUES	228%	35%	86%	30%	22%	16%	17%	16%	17%	16%	18%
EBITDA	**-11**	**33**	**3**	**37**	**95**	**159**	**164**	**198**	**206**	**231**	**118**
CHANGE (%)	-13%	-393%	-92%	1242%	157%	69%	3%	21%	4%	12%	-49%
MARGIN (%)	-126%	66%	15%	71%	78%	84%	83%	84%	83%	84%	82%
DEPRECIATION & AMORTIZATION	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
AS % REVENUES	2%	0%	1%	0%	0%	0%	0%	0%	0%	0%	0%
EBIT	**-12**	**33**	**3**	**37**	**94**	**159**	**164**	**198**	**205**	**231**	**117**
CHANGE (%)	-13%	-386%	-92%	1351%	158%	69%	3%	21%	4%	12%	-49%
MARGIN (%)	-128%	65%	14%	70%	78%	84%	83%	84%	83%	84%	82%
NET FINANCIAL INCOME/(EXPENSE)	**-5**	**-4**	**-4**	**-2**	**0**	**1**	**1**	**2**	**3**	**3**	**4**
PROFIT BEFORE TAXES	**-16**	**29**	**-2**	**35**	**94**	**160**	**165**	**199**	**208**	**234**	**122**
MARGIN	-179%	57%	-10%	67%	78%	84%	84%	85%	84%	85%	85%
TAXES	**0**	**-2**	**-3**	**-8**	**-35**	**-55**	**-57**	**-67**	**-70**	**-78**	**-43**
TAX RATE (%)	0%	8%	-165%	24%	37%	34%	34%	34%	34%	33%	35%
NET PROFIT/LOSS	**-16**	**26**	**-5**	**27**	**59**	**105**	**108**	**132**	**138**	**156**	**79**
CHANGE (%)	-7%	-263%	-118%	-647%	123%	76%	4%	22%	4%	13%	-49%
MARGIN (%)	-179%	52%	-27%	51%	49%	55%	55%	56%	56%	57%	55%
PROFIT/(LOSS) PER SHARE (IN EUR)	**-0.91**	**1.48**	**-0.27**	**1.49**	**3.33**	**5.87**	**6.07**	**7.39**	**7.72**	**8.74**	**4.42**
PROFIT/(LOSS) PER SHARE (IN CHF)	**-0.88**	**1.42**	**-0.26**	**1.43**	**3.19**	**5.62**	**5.82**	**7.09**	**7.40**	**8.37**	**4.24**
ESTIMATES AS OF 25 MARCH 2024										SOURCE: VALUATIONLAB ESTIMATES	

NOTE: At the end of FY 2023, Newron had a total of EUR 299 mn tax loss carryforwards, which the company can use on current and future profits.

Ratios & Balance Sheet

NEWRON PHARMACEUTICALS									SHARE PRICE (CHF)		7.50
RATIOS	**2023**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**	**2033E**
P/E		**5.3x**	**-28.7x**	**5.3x**	**2.4x**	**1.3x**	**1.3x**	**1.1x**	**1.0x**	**0.9x**	**1.8x**
P/S		**2.8x**	**7.7x**	**2.7x**	**1.2x**	**0.7x**	**0.7x**	**0.6x**	**0.6x**	**0.5x**	**1.0x**
P/NAV		**-40.0x**	**-16.7x**	**7.7x**	**1.8x**	**0.8x**	**0.5x**	**0.3x**	**0.2x**	**0.2x**	**0.2x**
EV/EBITDA		**3.8x**	**46.4x**	**3.5x**	**1.3x**	**0.8x**	**0.8x**	**0.6x**	**0.6x**	**0.5x**	**1.1x**
PER SHARE DATA (CHF)	**2023**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**	**2033E**
EARNINGS	**-0.88**	**1.42**	**-0.26**	**1.43**	**3.19**	**5.62**	**5.82**	**7.09**	**7.40**	**8.37**	**4.24**
CHANGE (%)	-14%	-261%	-118%	-647%	123%	76%	4%	22%	4%	13%	-49%
CASH	**0.68**	**2.62**	**2.29**	**2.63**	**8.09**	**17.10**	**26.39**	**37.54**	**49.14**	**62.16**	**69.15**
CHANGE (%)	-49%	284%	-13%	15%	208%	111%	54%	42%	31%	27%	11%
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	**-1.62**	**-0.19**	**-0.45**	**0.98**	**4.17**	**9.79**	**15.61**	**22.69**	**30.09**	**38.46**	**42.70**
CHANGE (%)	98%	-88%	139%	-318%	325%	135%	59%	45%	33%	28%	11%
BALANCE SHEET (EUR MN)	**2023**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**	**2033E**
NET LIQUID FUNDS	**13**	**49**	**43**	**49**	**151**	**318**	**492**	**699**	**915**	**1,158**	**1,288**
TOTAL ASSETS	**30**	**66**	**60**	**67**	**168**	**336**	**509**	**717**	**933**	**1,175**	**1,305**
SHAREHOLDERS' EQUITY	**-30**	**-3**	**-8**	**18**	**78**	**182**	**291**	**423**	**560**	**716**	**795**
CHANGE (%)	113%	-88%	139%	-318%	325%	135%	59%	45%	33%	28%	11%
RETURN ON EQUITY (%)	54%	-756%	58%	146%	76%	57%	37%	31%	25%	22%	10%
FINANCIAL DEBT	**26**	**48**	**36**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
FINANCIAL DEBT AS % OF TOTAL ASSETS	86%	72%	60%	0%	0%	0%	0%	0%	0%	0%	0%
EMPLOYEES	**22**	**22**	**23**	**23**	**24**	**24**	**25**	**25**	**26**	**26**	**27**
CHANGE (%)	0%	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%
CASH FLOW STATEMENT (EUR MN)	**2023**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**	**2033E**
NET PROFIT / (LOSS) BEFORE TAX	**-16**	**29**	**-2**	**35**	**94**	**160**	**165**	**199**	**208**	**234**	**122**
DEPRECIATION & AMORTIZATION	0	0	0	0	0	0	0	0	0	0	0
OTHER NON-CASH ITEMS	4	6	6	6	6	6	6	6	6	6	6
CASH FLOW	**-12**	**35**	**4**	**41**	**100**	**166**	**171**	**205**	**214**	**240**	**128**
NET INCREASE/(DECREASE) IN WORKING CAPITAL	2	2	2	2	2	2	2	2	2	3	3
OPERATING FREE CASH FLOW	**-10**	**36**	**6**	**42**	**102**	**168**	**173**	**208**	**216**	**243**	**130**
NET CASH FLOWS FROM INVESTING ACTIVITIES	3	0	0	0	0	0	0	0	0.0	0.0	0.0
NET CASH USED IN OPERATING ACTIVITIES	**-7**	**36**	**6**	**42**	**102**	**168**	**173**	**208**	**216**	**243**	**130**
NET CASH FLOWS FROM FINANCING ACTIVITIES	0	0	-12	-36	0	0	0	0	0	0	0
NET INCREASE/(DECREASE) CASH & CASH EQUIVALENTS	**-7**	**36**	**-6**	**6**	**102**	**168**	**173**	**208**	**216**	**243**	**130**

ESTIMATES AS OF 25 MARCH 2024 SOURCE: VALUATIONLAB ESTIMATES

NOTE: Newron's total available cash resources, including EUR 12.6 mn in cash and cash equivalents (31 December 2023), royalty income from Xadago sales, Italian R&D tax credits, the recent share subscription agreement with an institutional healthcare investor with up to EUR 15 mn in funding, and the deferral of the first three tranche payments of the EUR 40 mn EIB loan by roughly 1 ½ year, will finance its planned development programs and operations well into 2025 and beyond key value inflection points.

APPENDIX

I) LICENSING AGREEMENTS:

1) Meiji Seika's agreement for safinamide in Japan and key Asian territories in 2012

In April 2012, Newron signed an agreement with Meiji Seika (Meiji) covering the R&D, manufacturing, and marketing of safinamide (branded Equfina by Meiji) in Japan and key Asian territories. An upfront fee of EUR 5 mn was paid, with Newron eligible for undisclosed royalties on net sales (we conservatively assume a royalty rate of 2.5%). In 2017, Meiji and Eisai entered into a licensing agreement for safinamide in Japan and Asia. Eisai obtained exclusive rights to market safinamide in Japan and to develop and market in Asia (South Korea, Taiwan, Brunei, Cambodia, Laos, Malaysia, and the Philippines). Meiji continued the clinical trials it conducted and submitted a manufacturing and marketing authorization application in Japan. Eisai conducted clinical trials and made applications for regulatory approval in Asia. Meiji manufactures and supplies safinamide to Eisai for Japan and Asia. Meiji received an upfront payment from Eisai, as well as developmental milestones and sales royalty payments.

2) Zambon strategic collaboration & license agreement for Xadago in 2012

In May 2012, Newron entered into a strategic collaboration and license agreement for safinamide (branded Xadago by Zambon in Europe and the US), with Zambon responsible for safinamide research, development, manufacturing, and marketing in all territories of the world, excluding the Meiji territories (Japan and Asia). Zambon made a USD 25.5 mn investment in Newron and covered the costs of clinical development and preparing the application for marketing approval in Europe and the US. Newron received success-based regulatory milestone payments and is eligible for customary double-digit royalty payments on net sales of Xadago (we conservatively assume a tiered royalty rate of 10-12% in Europe/ROW).

In 2021, Newron agreed to a potentially pivotal trial to evaluate the efficacy of Xadago in Parkinson's disease patients with levodopa-induced dyskinesia (PD-LID). In March 2022, Newron and Zambon discontinued their plans to start a label extension trial for Xadago in PD-LID.

3) US commercialization of Xadago initially by US WorldMeds and now Supernus

In March 2016, Zambon signed a strategic agreement with US WorldMeds to commercialize Xadago in the US. Zambon is eligible for upfront, regulatory, and commercial milestone payments and royalties on Xadago sales. Newron received a milestone payment from Zambon when Xadago received FDA approval and is eligible for a share of the sales milestones and royalty payments made by US WorldMeds to Zambon (we conservatively assume a royalty rate of ~7% in the US)

In April 2020, Supernus Pharmaceuticals acquired the CNS portfolio of US WorldMeds, including the US rights to Xadago, and is now responsible for the US commercialization of Xadago.

II) EVENAMIDE CLINICAL DATA:

Evenamide has been evaluated in ~430 patients, consisting of ~160 healthy volunteers and ~270 schizophrenia patients in 9 clinical trials. 275 patients completed the trials, with ~130 patients in ongoing trials, including extension trials, with 24 patients discontinuing treatment, of which 4 were for adverse events (seizure, atrial fibrillation, vomiting, somnolence) and the remainder for other reasons. The most frequent (>3%) adverse events in the ~160 healthy volunteers included headache (7.5%), dizziness (6.3%) and abdominal pain/discomfort (3.1%). In the ~270 schizophrenia patients, the most frequent (>3%) adverse events included somnolence (5.5), headache (3.7%) and insomnia (3.3%).

SCHIZOPHRENIA:

POC TRIAL - Good tolerability and safety with preliminary evidence of efficacy
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 in March 2017. Evenamide met the trial objectives of good tolerability and safety and showed preliminary evidence of efficacy.

The 4-week, double-blind, placebo-controlled, randomized, multinational phase IIa POC trial was designed to assess the safety, tolerability, and early evidence of efficacy of evenamide as an add-on treatment in 89 patients diagnosed with 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 a placebo on top of their current antipsychotics.

Well tolerated on top of the 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 an SAE. In the patient with atrial fibrillation, the highest concentration of evenamide was ~11-18 fold less than 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 of 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 schizophrenia symptoms

The results of the POC trial showed a benefit on all measures assessed. Patients treated with evenamide showed improvement in 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 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).

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

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 the 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.

SHORT-TERM EXPLANATORY STUDIES:

Required by the FDA before starting phase III underline a 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 the 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, that 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 arrhythmia), 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 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 FDA requested the trial to address questions that 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 on 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 was 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.

TREATMENT-RESISTANT SCHIZOPHRENIA (TRS):

"STUDY 014/015" - Final FDA safety trial required to start pivotal development in TRS
The phase II "Study 014" and long-term 1-year extension trial "Study 015" is the final safety

trial required by the FDA before starting the pivotal phase III "Study 017" of evenamide in TRS, including clozapine treatment-resistant schizophrenia (CTRS). "Studies 014/015" is an international, randomized, open-label, rater-blinded trial of evenamide as an add-on to an antipsychotic (excluding clozapine) in patients with moderate to severe treatment-resistant schizophrenia who were no longer responding to their current antipsychotic medication.

The primary objective of "Study 014" is to evaluate the safety and tolerability of evenamide in three oral fixed doses of 7.5 mg, 15 mg, and 30 mg twice daily (BID) for 6 weeks in patients with TRS. The secondary objective is the assessment of preliminary efficacy that includes the changes from baseline in the Positive and Negative Syndrome Scale (PANSS) total score, Clinical Global Impression of Change (CGI-C) and Severity of Illness (CGI-S), Strauss-Carpenter Level of Functioning (LOF), and Medication Satisfaction Questionnaire (MSQ), among others.

Positive topline results of "Study 014" – Excellent tolerability and safety

On 20 March 2023, compelling topline results were announced for "Study 014", a phase II, international, randomized, open-label, rater-blinded trial evaluating evenamide as an add-on to an antipsychotic (excluding clozapine) in 161 patients with moderate to severe treatment-resistant schizophrenia (TRS) not responding to their current antipsychotic medication, which showed a statistically significant improvement over baseline in all efficacy measures at the 6-week primary endpoint. These results are consistent with previously reported interim data from the first 100 patients after 6-week treatment, reported in June 2022 (see below). Detailed results of "Study 014" were presented at the European College of Neuropsychopharmacology (ECNP) Congress in Barcelona, Spain, in October 2023.

Primary endpoint of safety established showing excellent tolerability and safety

Of the 161 patients who were randomized, 153 (95%) completed the 6-week treatment period, and 144 (94% of the completers) entered the extension trial "Study 015" for further treatment of up to one year. One patient discontinued treatment due to flu-like symptoms, and seven withdrew consent. The number of patients who experienced treatment-emergent adverse events (TEAEs) was low (26%), and none was rated severe. The most commonly reported TEAEs (≥3%) were dizziness, pyrexia (fever), and creatine phosphokinase (CPK) increase (potential injury or stress to muscle tissue). No treatment-emergent or clinically important findings for weight gain, metabolic syndrome, sexual dysfunction, neurological findings (based on ESRS-A and neurological examination), standard laboratory tests or electrocardiograms (ECGs) were reported. This adverse event profile was also similar to that seen from the first 100 patients.

Preliminary efficacy signals across all scores and similar to prior interim data

The mean Positive and Negative Syndrome Scale (PANSS) total score, Clinical Global Impression of Severity (CGI-S) rating, and the Strauss-Carpenter Level of Functioning (LOF) total score significantly improved compared to the baseline ($p<0.001$). The proportion of patients considered "clinically important responders" on the PANSS, the Clinical Global Impression of Change (CGI-C), and the CGI-S was in line with the proportion of the first 100 patients experiencing this level of benefit after six weeks. The mean improvement from baseline was also consistent for the Medication Satisfaction Questionnaire (MSQ) when compared to this measure for the first 100 patients.

The results indicate that the last 61 patients to be enrolled in "Study 014" share the same

demographic and disease improvement characteristics as the first 100 patients after 6-week treatment. Treatment with evenamide at all doses of 7.5 mg, 15 mg, or 30 mg twice-daily (BID) was also as well tolerated in the final 61 patients as was shown in the initial cohort of 100 patients, thus confirming the reliability of the data collected in this trial. Most importantly, the pattern of benefit associated with evenamide in these 61 patients was similar to the efficacy noted in the first 100 patients, without any evidence of systematic differences between doses of evenamide. Additionally, the efficacy benefits of evenamide in the analysis of all 161 patients at six weeks appeared very similar to the findings from the first 100 patients. The tolerability and safety of the doses of evenamide in the last 61 patients were also largely similar to that reported earlier in terms of high completion rate, low discontinuation due to adverse events, and a very low incidence of adverse events.

"Study 015" 1-year results show unprecedented efficacy, with ~25% of TRS patients in remission (cure) and >70% experiencing a meaningful reduction in disease severity

On 4 January 2024, Newron reported unprecedented efficacy results of the open-label (unblinded) "Study 015" 1-year extension trial of the 6-week phase II "Study 014" safety and dose-ranging trial of evenamide as an add-on to current antipsychotics in treatment-resistant schizophrenia (TRS) patients. Evenamide was safe and well-tolerated at one-year treatment in TRS patients, with >70% of patients experiencing a clinically meaningful reduction in disease severity, ~50% of patients no longer meeting any of the TRS protocol severity criteria, and ~25% of patients achieving remission (cure), which has never been seen before in this treatment population. Moreover, the clinically significant benefit of evenamide was sustained and increased throughout the one-year treatment course. The increasing benefit over time from six weeks to one year suggests that the glutamate-modulating effect of evenamide could lead to a progressive and long-standing alteration in brain processes synergizing with the effect of antipsychotics to which the patient had become resistant with the potential to transform the management and societal outlook for these difficult to treat TRS patients.

"Study 014/015" was the final safety trial required by the FDA to start a pivotal phase III trial. The EMA, FDA, and Canada have agreed upon the trial design of the potentially pivotal phase III trial dubbed "Study 017" (previously named "Study 003"), a 12-week, double-blind, randomized, placebo-controlled trial in more than 510 patients with TRS. If "Study 017" replicates the exceptional efficacy results seen in "Study 014/015", approval in TRS should follow swiftly based on this single pivotal trial alone. TRS provides a large market opportunity representing more than 30% of the schizophrenia population.

Final results indicate evenamide can be safely added to current antipsychotic therapy

The final results of "Study 015" at one-year treatment indicate that adding evenamide to antipsychotics (excluding clozapine) was well tolerated, with a low incidence of treatment-emergent adverse events (TEAEs), and without any pattern of motor or central nervous system (CNS) symptoms, weight gain, sexual dysfunction, or laboratory/electrocardiogram (EKG) abnormalities (a major concern of the FDA). The favorable safety profile of evenamide indicates it could be added to any current antipsychotics in patients with schizophrenia without the risk of drug-to-drug interaction or additional toxicity.

Safe and well tolerated, with less than 30% of patients experiencing a side effect

Of the 161 TRS patients randomized in the trial, 121 (75%) completed one year of treatment. A total of 31 patients (19%) discontinued due to withdrawal of consent (23 patients), not rolling over into the 1-year extension trial "Study 015" after completing the 6-week "Study

014" (9 patients), lost to follow up (5 patients), and adverse events (3 patients). Less than 30% of patients experienced at least one treatment-emergent adverse event (TEAE). Two serious adverse events (SAEs) were reported: 1 death with autopsy findings suggestive of atherosclerosis and 1 patient with dilutional hyponatremia (water intoxication) followed by an acute symptomatic seizure that occurred beyond 1 year of treatment. There is no pattern of extrapyramidal side effects, endocrine or metabolic syndrome, sexual dysfunction, significant CNS events, or laboratory abnormalities. No patient relapsed during one year of evenamide treatment.

Key efficacy findings of "Study 015" after one year of treatment with evenamide

"Study 015" is the 1-year extension trial of the six-week open-label (unblinded) "Study 014" safety and dose-ranging trial (twice-daily 7.5 mg, 15 mg, or 30 mg evenamide, no placebo) that determined the long-term benefits of glutamate release inhibition by adding evenamide to current antipsychotics (excluding clozapine). The preliminary efficacy assessment was based on changes from baseline in the Positive and Negative Syndrome Scale (PANSS). Changes from baseline in the Clinical Global Impression of Change (CGI-C), Severity of Illness (CGI-S), and Strauss-Carpenter Level of Functioning (LOF) scale were secondary objectives. Despite these patients being on therapeutic doses of antipsychotics, the PANSS total score, the CGI-S, and the LOF all showed a statistically significant improvement at one year of evenamide treatment (p-value < 0.001: paired t-test, OC/LOCF) in the modified intent-to-treatment (mITT) population. Moreover, all efficacy scales showed gradual and sustained improvement over the treatment period.

- **Treatment response – PANSS total score (primary efficacy objective):**
  - The mean change from baseline in the PANSS total score dropped by 15.5 points or 19.4% from 79.5 at baseline to 63.9 at one year of treatment.
  - The percentage of patients with a clinically important response (a PANSS total score ≥20% improvement from baseline) amounted to 41.8% of patients at one year of treatment (up from 34% at 6 months and 24.8% at 18 weeks)
  - Approximately 90% of the patients who had responded to the treatment by a clinically important reduction (≥ 20% from baseline) on the PANSS total score at six months (~45%) maintained their response at one year.
- **Disease severity – CGI-S (secondary efficacy objective):**
  - A 1.1-point drop was seen in the CGI-S mean change from baseline from 4.5 (moderate-to-severe disease) at baseline to 3.5 (mild-to-moderate disease) at one year of treatment.
  - 75.2% of patients experienced a clinically important reduction in disease severity (an improvement of ≥ 1-category from baseline) at one year of treatment (up from 74.5% at 6 months and 70.9% at 18 weeks).
  - The percentage of patients classified by the physician as "much improved" amounted to 37.6% at one year of treatment (up from 30.5% at 6 months and 27.0% at 18 weeks)
- **Level of functioning – LOF (secondary efficacy objective):** a 2.4-point improvement was seen in the LOF mean change from baseline (up from 18.0 at baseline to 20.4 at one year of treatment).
- **Relapse:** no patient relapsed during the one-year treatment period with evenamide, in contrast to common clinical experience.
- **TRS protocol severity criteria:** a review of the efficacy data indicated that treatment with evenamide resulted in approximately 50% of patients at one year no longer meeting

any of the protocol severity criteria used to diagnose treatment resistance.

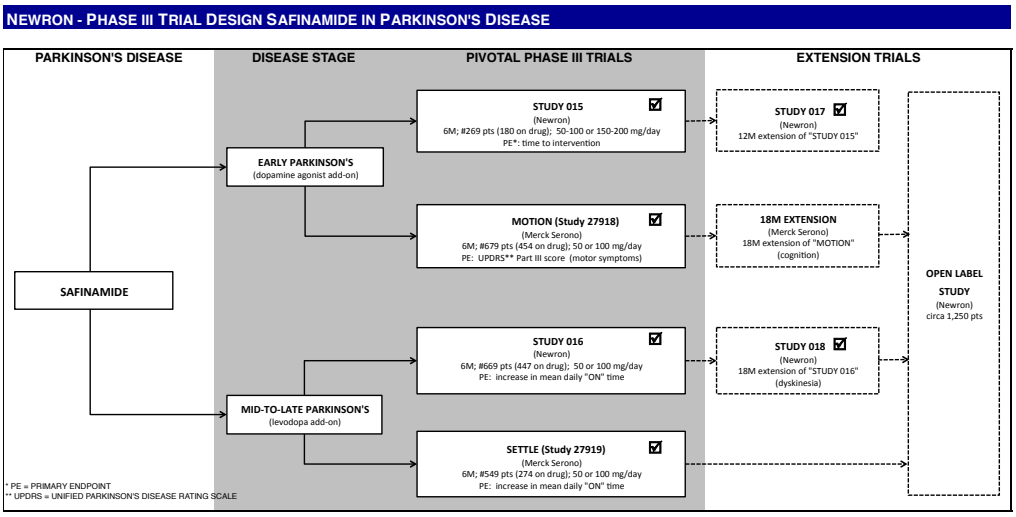
- **Remission:** approximately 25% of all patients achieved remission, defined as a level of symptomology that does not interfere with an individual's behavior and is also below that required for a diagnosis of schizophrenia. Remission represents the highest level of improvement that can be obtained in a patient with schizophrenia. Remission in TRS patients has never been seen before.

III) XADAGO CLINICAL DATA:

The EU and US approvals of Xadago (safinamide) in Parkinson's disease were based on an extensive clinical development program that included over 1,500 patients, of whom around 1,000 were treated for at least one year and many for over four years. Efficacy was derived from five placebo-controlled studies, including assessments performed under double-blind conditions for two years.

Xadago was developed for all disease stages of Parkinson's disease:

1) **Early-stage disease** as an add-on to dopamine agonists (approximately 20% of patients)
2) **Mid-to-late-stage disease** as an add-on to levodopa and other dopaminergic treatments (approximately 80% of patients)



SOURCE: VALUATIONLAB, NEWRON PHARMACEUTICALS

This is reflected in the phase III trial design, with all 4 phase III trials reaching their primary endpoint. Newron has also performed extension trials. Although they were not necessary for approval, they provide an important insight into the long-term impact of Xadago, including demonstrating long-term efficacy and anti-dyskinetic properties.

Statistically significant results in early-stage Parkinson's disease...

Xadago demonstrated statistically significant results as an add-on to a single dopamine agonist in three placebo-controlled trials in early Parkinson's disease. Note that the positive effects are on top of dopamine agonists that already provide efficacy in early Parkinson's disease. Roughly 30% of Parkinson's patients are on dopamine agonists.

UPDRS II/III primary endpoint met in "Study 015" and "MOTION"

The primary endpoint of both studies was the so-called UPDRS, the Unified Parkinson's Disease Rating Scale, Part II and III. This is a rating tool used to follow the longitudinal

course of Parkinson's disease. It comprises five sections, with **Part II** being a self-reported evaluation of activities of daily living (ADL) and **Part III** a clinician-scored motor evaluation. In the first pivotal phase III, **"Study 015"**, the low dose range (50-100 mg/day) showed a mean change from baseline of -2.2 (p=0.0248) for UPDRS II and -6.00 for UPDRS III at 6 months. In the 12-month extension "Study 017", there was a mean change from baseline of -4.7 for UPDRS III and a responder rate of 18.1% difference from placebo at 18 months, as well as statistically significant benefits on UPDRS II and EuroQoL (quality of life).

In the second pivotal phase III **"MOTION"** trial the 100 mg/day dose showed a -2.06 (p=0.0396) mean change from baseline on UPDRS III at week 24, which was statistically significant (p=0.040) compared to the placebo group that showed a mean change from baseline of -1.04 in the DA-ITT (dopamine agonist intent-to-treat) population. The 50 mg/day showed a -1.93 mean change from baseline that did not reach statistical significance compared to placebo.

Patients and physicians see improvements in quality of life scores
In two other secondary endpoints, the **EQ-5D** (patient scored European Quality of Life index) and the **PDQ-39** (patient scored Parkinson's Disease Quality of Life index), the 100 mg/day dose of Xadago reached statistical significance as well.

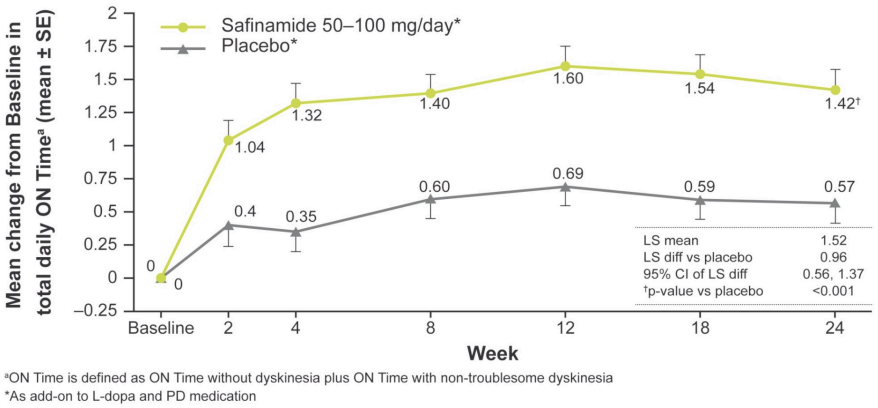
Adding 100 mg of Xadago on top of a dopamine agonist in early Parkinson’s disease statistically improves motor fluctuations and activities of daily living (physician-rated), and several quality-of-life scores were recorded in both caregiver and patient evaluations.

Xadago was well-tolerated, with the majority of patients completing the trials
In both phase III trials, Xadago was well-tolerated, with most side effects similar to placebo, with almost all patients (approximately 90%) completing the trials. In the "MOTION" trial, nausea (9.7% vs. 6.7%) at the 100 mg/day dose occurred more frequently in the Xadago group compared to the placebo group, and dizziness (8.0% vs. 6.2%) at the 50 mg/day dose. Drowsiness and back pain (4.8% vs. 8.0%) were lower than placebo with Xadago 100 mg/day.

...as well as in mid-to-late-stage Parkinson's disease
Xadago also showed statistically significant results in its two pivotal phase III trials as an add-on to stable doses of levodopa and/or other stable dose dopamine agonists/anticholinergics in mid-to-late-stage Parkinson's disease. Roughly 70-80% of PD patients are on levodopa regimens.

Daily ON-time primary endpoint met in "Study 016" and "SETTLE"
The primary efficacy endpoint was to evaluate the change from baseline to week 24 in daily ON-time (ON-time without dyskinesia plus ON-time with non-troublesome dyskinesia)
In the first pivotal phase III **"Study 016",** both the 50 and 100 mg doses met the primary endpoint of improving ON-time (+0.6 hours vs. placebo, p=0.02 at 50 mg, p=0.013 at 100 mg). Importantly, the increase in ON-time was not associated with any increase in troublesome dyskinesia. Key secondary endpoints were also met, including **OFF-time**,

UPDRS III, and **PDQ-39** at 6 months. A consistent result occurred in the second pivotal phase III **"SETTLE"** trial where Xadago showed a significant improvement in its primary endpoint of ON-time of almost an hour (+0.96 hours vs. placebo, p<0.001).



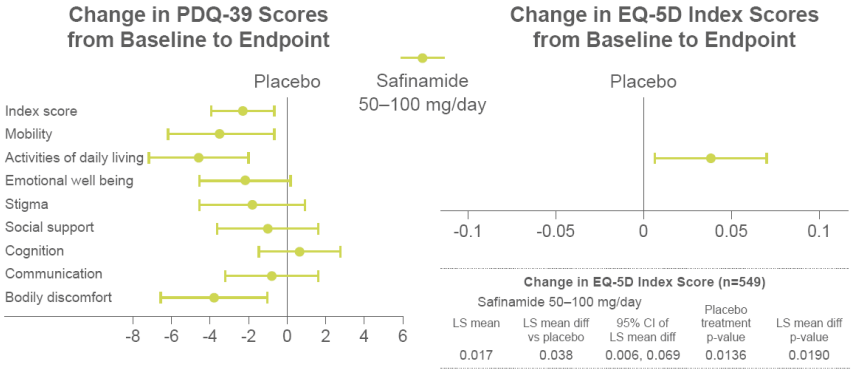
[a]ON Time is defined as ON Time without dyskinesia plus ON Time with non-troublesome dyskinesia
*As add-on to L-dopa and PD medication

SOURCE: NEWRON PHARMACEUTICALS

In the graph above, one can clearly see that adding Xadago (safinamide) on top of levodopa therapy adds approximately one-hour ON-time, already after two weeks, and this statistically significant effect is continued throughout the trial. Importantly, the increase in ON-time was not associated with any increase in troublesome dyskinesia.

...and patients and physicians see improved quality of life scores and less OFF-time

Statistically significant results in secondary endpoints were also reported, including total daily **OFF-time** (-1.03 hours vs. placebo, p<0.001), mean change from baseline in **UPDRS III** during ON-time phase (-1.82 vs. placebo, p=0.003), **PDG-39** (-2.33, p=0.006) and **EQ-5D** (0.06, p<0.001) scores, and in **OFF-time post morning dose of levodopa**. The latter is important for patients and caregivers as PD patients are often "frozen" in the morning, requiring immediate-release levodopa.



SOURCE: NEWRON PHARMACEUTICALS

In the graphs above, one can clearly see that adding Xadago (safinamide) to levodopa therapy improves a broad range of scores that improve patient's quality of life and daily activities.

"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 were 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, in "Study 016/018" showed under double-blind, placebo-controlled conditions that Xadago (safinamide) 100 mg/day reduces dyskinesia. Currently, there are no drugs on the market that have shown to reduce dyskinesia over such a period.

Xadago is an MAO-B inhibitor with unique and attractive qualities

Although rasagiline (branded Azilect by Teva) and Xadago 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 mid-to-late-stage Parkinson's disease. 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 of 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 into 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)

The difference in safety and tolerability is apparent when we compare Xadago and Azilect based on the US prescribing information provided by the FDA.

ADVERSE EVENTS COMPARISON

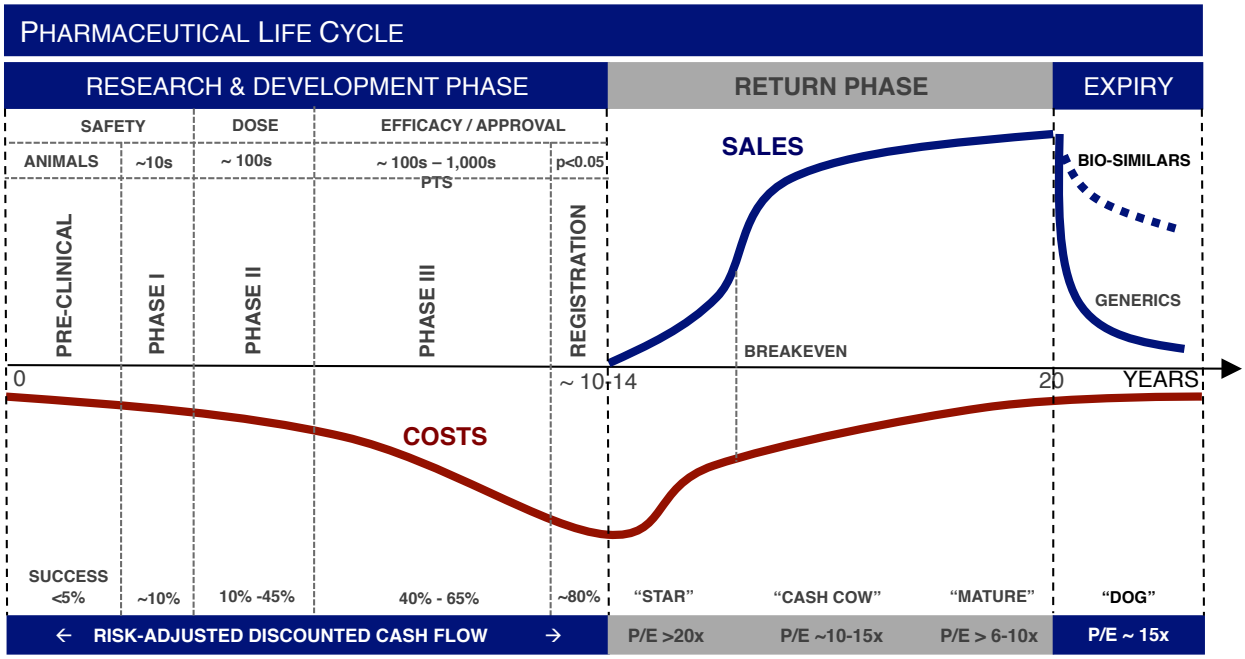
ADVERSE EVENTS > 2%	AZILECT "STUDY 3" (+ L-DOPA); 26 WEEKS			XADAGO "STUDIES 1 & 2" (+ L-DOPA); 24 WEEKS		
	1 MG/DAY (N=149) (%)	0.5 MG/DAY (N=164) (%)	PLACEBO (N=159) (%)	50 MG/DAY (N=223) (%)	100 MG/DAY (N=498) (%)	PLACEBO (N=497) (%)
DYSKINESIA (UNCONTROLLABLE MOVEMENT)	**18**	**18**	10	**21**	**17**	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, Xadago has fewer 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 at a similar rate as with Azilect and is mostly transient in nature when therapy is started. Regarding 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.

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

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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.

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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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