Newron Pharmaceuticals - Developing novel treatments for CNS diseases and pain (SIX: NWRN)

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CEO

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Newron Pharmaceuticals: Developing treatments for patients with debilitating Central Nervous System diseases

- **Parkinson’s disease**: Xadago® (safinamide)
  - Marketing Authorization in the EU and Switzerland in 2015
  - Launched in 8 European markets
  - US: Response to FDA CRL letter submitted; meeting planned

- **Schizophrenia**: Evenamide® (NW-3509)
  - Phase II placebo-controlled study in schizophrenic patients ongoing

- **Rett syndrome**: Sarizotan
  - Phase III potentially pivotal study approved by FDA and EMA
  - Study start in Q3/2016
## Innovative Therapies for CNS Disease and Pain

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<td>Rett syndrome (Orphan drug status)</td>
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\(^1\) Safinamide, NW-3509 and Ralfinamide all developed from Newron’s ion channel based research

\(^2\) Sarizotan was licensed from Merck Germany
Achievements in Past 12 Months

• Xadago® (safinamide)
  – Launched in 7 EU countries and Switzerland by Zambon
  – CRL received on March 29, 2016 (PDUFA date)
  – Response submitted in May, 2016, meeting planned
  – Phase III study initiated in Japan (Meiji Seika Pharma)

• Sarizotan
  – ODD for the treatment of patients with Rett syndrome in EU and U.S.
  – IND approved May 2016
  – International Phase III potentially pivotal study planned in patients with Rett syndrome

• Evenamide (NW-3509)
  – US Phase II study started and ongoing in patients with positive symptoms of schizophrenia
## Xadago® (safinamide): First NCE Approved for PD in a Decade

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| Safinamide | Adjunctive therapy in PD | Adjunctive therapy in PDM | Adjunctive therapy in PD | Adjunctive therapy in PD | | Zambon  
US Worldmeds  
Meiji Seika |
Parkinson’s disease (PD) affects 7 -10 million people worldwide.

Degenerative disorder of the CNS impairing patients’ motor skills, cognitive processes, behaviour and speech.

Standard of treatment is with levodopa, with or without addition of dopamine agonists.

Treatment with L-dopa leads to motor fluctuations (ON or OFF-time) and involuntary movements known as L-dopa-Induced Dyskinesia (LID).
Xadago® (safinamide): First NCE Approved for PD in a Decade

First PD therapy working through dual mechanism

Once daily oral adjunctive therapy for patients with PD

- Alpha-amino amide derivative, high solubility and bioavailability
- Early onset of action and benefits seen in patients for over 2 years
- Significant increase in “Responder Rates” compared with standard of care
- Current PD treatments only enhance dopaminergic function
- Xadago (safinamide)
  - Enhances dopaminergic function
  - Reduces glutamatergic release (with potential to reduce dyskinesia)

Efficacy and safety demonstrated as add-on to

- Dopamine agonists (early PD)
- L-dopa (mid to late stage PD)
Xadago® (safinamide) Offers Multiple Benefits to PD Patients

**Early PD Patients** – add to dopamine agonist

- Significant improvement of
  - UPDRS III - motor function, regulatory endpoint (mean change, responder rate)
  - Quality of life (PDQ-39, EQ5D)
- Reduction of number of interventions (first time use of L-dopa)
- Benefits seen after 6 and 18 months
- Delay levodopa

**Mid- to late-stage PD Patients** – add to dopamine replacement

- Significant improvement of
  - ON Time/OFF Time – regulatory endpoint
  - UPDRS II – activities of daily living/UPDRS III – motor function
  - UPDRS IV – treatment complications
  - CGI (Clinical Global Impression) – Severity and Improvement
  - Increase in clinically significant response (ON time, OFF time, UPDRS III), response rates over standard of care
- Additional ON Time Without Any Increase In Any Dyskinesia
- Dyskinesia significantly improved
- Benefits seen after 6 and 24 months

**Long Term Duration of Effect**

**ON Time** (without troublesome dyskinesia) - Change from Baseline

![Graph showing long term duration of effect on ON time](image)
Xadago® (safinamide): Commercial Opportunity

- Long lasting market exclusivity (patent life: 2029 in EU, 2030 in the U.S.)
- Milestone and royalty revenues to Newron since 2012
- Peak sales potential $450m - $700m+ (analyst estimates)

Identifying further parties for regional sublicensing

Countries covered:
- EU
- Latin America
- U.S.
- Canada
- Australia
- Japan
Milestones

- Xadago® (safinamide) has already been launched in (Germany, Switzerland, Italy, Spain, Belgium, Denmark, Sweden, UK)
- Further EU launches expected in 2016
- On US PDUFA date (March 29, 2016), Newron received Complete Response Letter
  - No need for additional efficacy or safety studies
  - Assessment of abuse liability and dependence/withdrawal effects needed
- Type A meeting with FDA/CSS to confirm Newron’s response to CRL
- Xadago® (safinamide) has the potential to assist the more than one million Americans currently living with Parkinson's disease
**Evenamide (NW-3509) – Voltage gated sodium channel blocker for Schizophrenia**

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Evenamide (NW-3509) for treatment of symptoms of Schizophrenia

- Onset of disease occurs in teenage years in males, and 5 years later in females: need for lifelong treatment; affects 1% of the population worldwide*
- Disease characterized by hallucinations, delusions, paranoia and disorganised speech
- Progressive deterioration of cognition, behaviour, thought disorder, and presence of negative symptoms
- High rates of suicidality, suicide, multiple physical illnesses, and lower life expectancy (at least 10 years on average)
- No new effective treatment that reduces burden of disease in last 20 years: large market opportunity (anti-psychotic market >$23bn)

Evenamide (NW-3509) acts by a new mechanism, improving treatment of Schizophrenia

- First in class voltage-gated sodium channel (VGSC) blocker for add-on treatment in schizophrenia, schizo-affective and bipolar disorders
- Novel small molecule, oral available, rapid onset of action, high availability in the brain
- Benefit shown in models of positive symptoms, aggression, cognition (schizophrenia), negative symptoms, mania, depression, obsessive behavior
- Potential to benefit patients showing inadequate response to current antipsychotics
- Phase I study completed
  - Drug was well tolerated
  - Exposure increased with dose
  - Exposure overlaps with exposure in animals at doses proven to be efficacious
- Phase II placebo-controlled study ongoing
Unique MOA: selective Voltage-Gated Sodium Channel (VGSC) Blocker

**Evenamide (NW-3509)**

- Selectively blocks VGSCs in a voltage-and use-dependent manner
- Modulates sustained repetitive firing without inducing impairment of the normal neuronal excitability
- Inhibits Glutamate Release

| Inhibition of naive sodium channels expressed in rat cortical neurons |
|--------------------------|--------------------------|
| **K_{rest} (μM)** | **K_{inact} (μM)** |
| 25 | 0.4 |

High frequency firing

Low frequency firing

Control

NW-3509 1μM
Phase II placebo-controlled study with Evenamide (NW-3509) as add-on in positive symptoms of schizophrenia

- NW-3509 as add-on treatment to patients with stable and adequate dose of standard therapy, experiencing break-through symptoms
- Double blind, placebo controlled, randomized, 4-week in/outpatient study in US and India in minimally 90 patients receiving Evenamide (NW-3509) 15-25 mg/daily (given BID) or placebo
- Selection Criteria:
  - Current diagnosis of schizophrenia in accordance with DSM-5
  - PANSS (Total) < 80; CGI-S rating of mildly, moderately, or moderately severely ill
  - Excludes patients with hallucinatory behavior, excitement, delusions, suspiciousness/persecution and hostility
  - Endpoints: Symptoms of schizophrenia, as assessed by
    - Positive and Negative Syndrome Scale (PANSS)
    - Clinical Global Impression - Change from baseline (CGI-C) and CGI - Severity of illness (CGI-S)
- Enrollment started: Jan 2016, results expected by end 2016
Sarizotan – Targeting respiratory disturbances in Rett syndrome

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Sarizotan for treatment of patients with Rett Syndrome

- Severe neurodevelopmental disorder primarily affecting females (1:10,000)
- Mutations in X-linked methyl CpG-binding protein 2 in majority of patients
- Causes severe disability, reduces life expectancy
- Normal development until 6-18 months of age, then lose fine motor skills, ability for social interaction, encounter cardiorespiratory dysregulation
- 60% survival at 37 years (vs. appr. 98%)
- Approx 70% of patients demonstrate respiratory abnormalities e.g. apnea, hyperventilation, respiratory dysrrhythmia
- 25% of sudden deaths in Rett linked to cardio-respiratory abnormalities
- Medication needed for breathing irregularities, motor difficulties, seizures’ control (anti-convulsant)
- No specific treatment approved for Rett Syndrome; focus on symptom management
Sarizotan has Potential to Treat Respiratory & Associated Symptoms

- Aminomethyl chromane derivative; new chemical entity
- Breathing disturbance in Rett syndrome postulated to involve neuronal hyperactivity in the brainstem (Raphe nucleus, Kölliker-Fuse nucleus, Bötzingen complex)
- Dramatic effect demonstrated on respiration in null mutant MeCP2 mouse model of Rett syndrome
- Potential additional benefits in other core features of Rett syndrome
Strategy for Regulatory Approval and Commercialization

- EU (Germany, Spain, UK) Health Authorities accepted proposed CMC/preclinical/clinical safety data package, agreed to single pivotal study: Q2/2015
- Similar agreements with Canadian (TPD) and U.S. (FDA): Q2-3/2015
- Orphan Drug Designations obtained in EU and U.S.: July 2015
- Efforts ongoing to extend treatment to younger patients: Interaction with EU Pediatric Development Committee Q3/2015
- Advocacy relationships being developed; Rett foundations for potential funding/co-sponsorship of activities
- ‘Rare Pediatric Disease’ voucher possibility

U.S.
16,000 patients
Orphan exclusivity
7.5 years post approval

EU
20,000 patients
Orphan exclusivity
12 years post approval
First ever Phase III potentially pivotal study in Rett syndrome (US IND); start in Q3/2016:
- Double-blind, randomized placebo-controlled, 28 week, multi-center design in approx. 120 patients
- Primary endpoint: Reduction in number of objectively defined apnea episodes

Initiation of Global Burden of Illness Caregiver Outreach Program

Partnering within the Rett community to solicit the views of caregivers in support of the unmet medical need (impact on health-related or general quality of life & resource utilization)

Health Economic Outcome Research study (HEOR) → “Burden of Illness” will support Health Technology Assessment (HTA); meets European Network of countries requirements to support pricing & treatment access
Milestones / News Flow

2016 / 2017

Xadago® (safinamide) in PD
• Market approval/launch
  – EU next launches: HY 2/2016
  – U.S. Meeting with CSS: Q3/2016

Evenamide (NW-3509) in Schizophrenia
• Phase II results Q4/2016
• License transaction

Sarizotan in Rett syndrome
• Phase III pot. Pivotal efficacy study initiate: Q3/2016
• Findings from the Burden of Illness study: 2017
• Results from Phase III pot. pivotal study: 2017
• Commercialization by Newron: 2018
### Financial Snapshot

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<th>Liquidity of Stock</th>
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<td>14,432,911</td>
<td>42,000/day</td>
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**Market Cap**  
240 Million CHF

**52-week**  
High: 31.35 CHF  
Low: 15.00 CHF

### Key Shareholders
- Investor AB
- Zambon
- Aviva
- JPMorgan AM
- Swisscanto
- Polar Capital
- Sphera Global Healthcare
- Nyenburgh
- Abingworth

### Analyst Coverage
- Charles Duncan, Piper Jaffray
- Bob Pooler, Valuation Lab
- Samir Devani, Rx Securities
- Susie Jana, Edison

**Shares Outstanding**: 14,432,911  
**Liquidity of Stock**: 42,000/day average trading volume (6mth)  
**Market Cap**: 240 Million CHF  
**52-week**  
High: 31.35 CHF  
Low: 15.00 CHF
Newron Pharmaceuticals: Highlights

• Innovative treatments for patients with debilitating CNS diseases with unmet medical needs
• Material revenues from Parkinson’s disease drug
• Pipeline opportunities
  – First therapy to be approved for patients with Rett Syndrome – to be commercialized by Newron
  – First add-on therapy to patients with positive symptoms of schizophrenia
• Experienced management team – CNS specialists
• Solid financial position