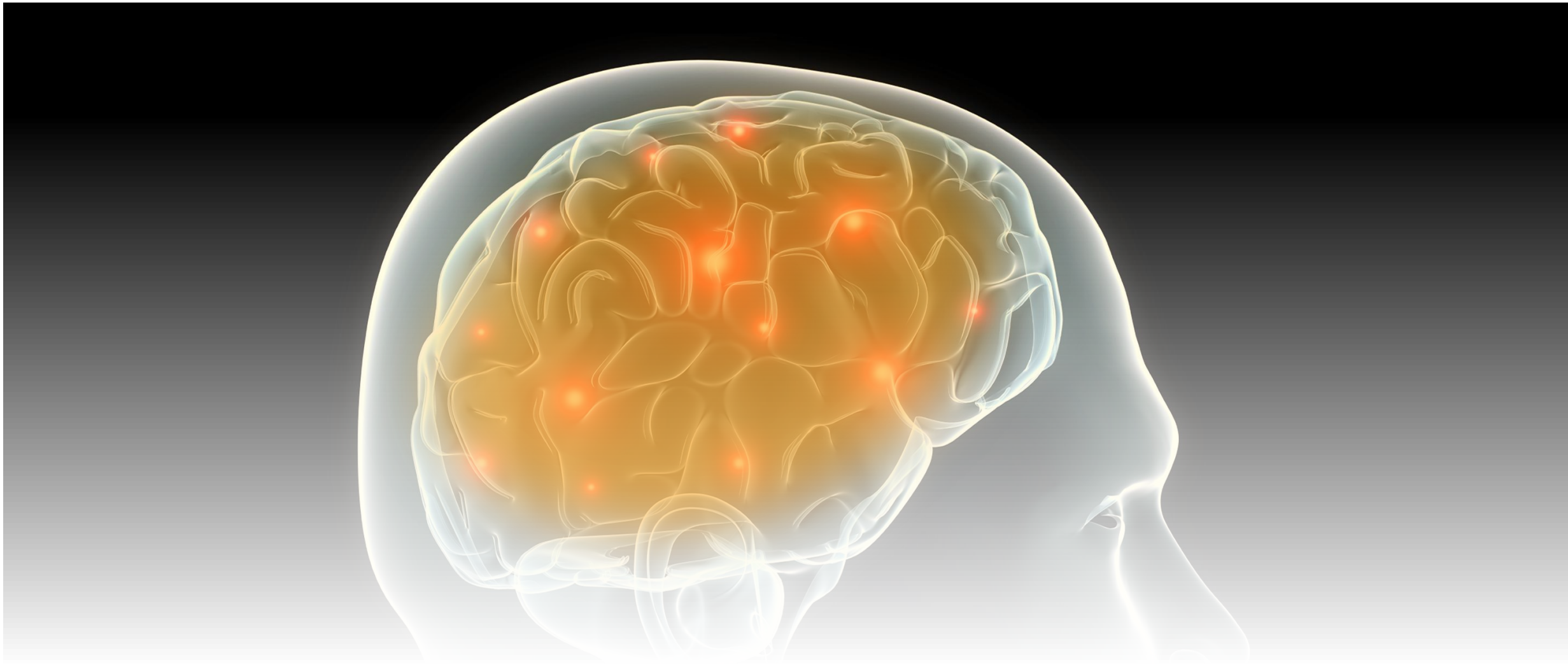
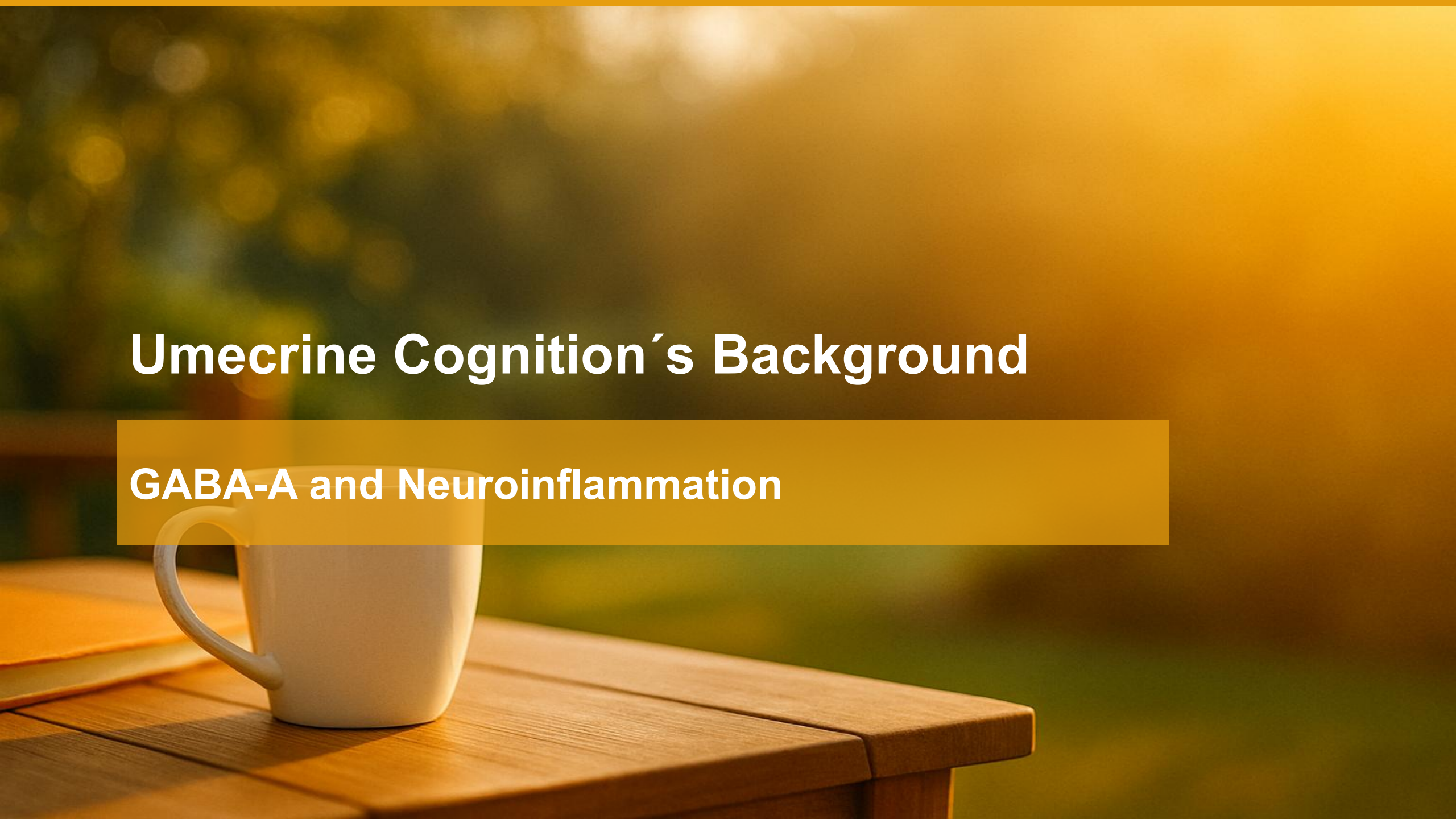
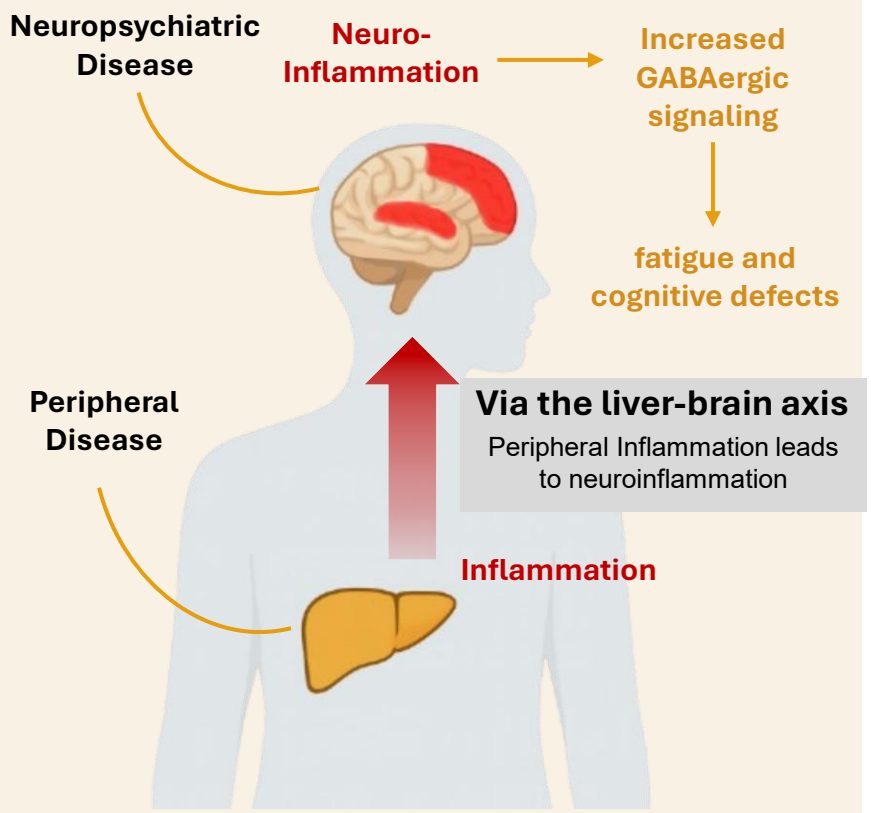


Umecrine cognition

Redeye 15 Oct 2025


Umecrine Cognition´s Background
GABA-A and Neuroinflammation

Liver-Brain Axis with Neuroinflammation



- **Many diseases trigger neuroinflammation** – from outside the brain (e.g. liver disease) or within the brain (e.g. Parkinson's, MS, Alzheimer's, ALS).
- **In many of these diseases neuroinflammation increase allopregnanolone**, a neurosteroid that disrupts brain balance.
- **Allopregnanolone overstimulates GABA-A receptors**, leading to impaired signaling.
- **This causes debiliating symptoms** like central fatigue, brain fog, and cognitive decline.

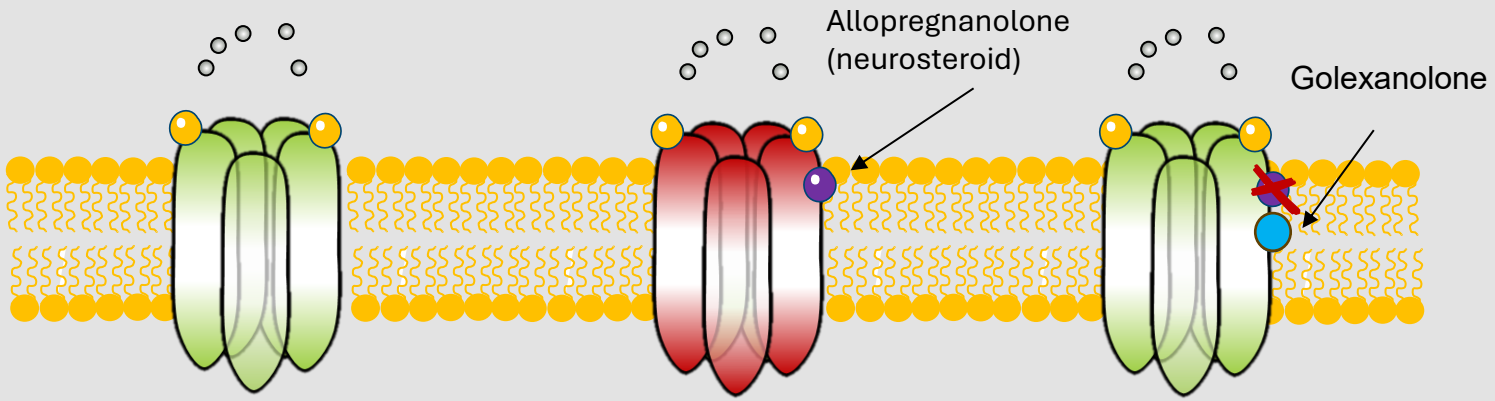
GABA-A Receptor and Neuroinflammation

GABA-A is the principal inhibitory receptor (ligand-gated Cl^- channel) that sets the brain's excitation–inhibition balance for alertness and cognition

1 Normal GABA-A signaling

2 Neuroinflammation raises allopregnanolone

3 Golexanolone normalizes inhibition



In neuroinflammation, allopregnanolone potentiates GABA-A—especially extrasynaptic (tonic) receptors—driving persistent over-inhibition.

- Over-inhibition presents as **central fatigue, brain fog, and daytime sleepiness.**
- Umecrine Cognition focuses on **neuroinflammation-driven by GABA-A overactivation** in indications with elevated allopregnanolone.
- Golexanolone antagonizes neurosteroid action at GABA-A, **restoring balanced signaling without full receptor block.**

Primary Biliary Cholangitis

A promising orphan entry

Summary of Clinical Evidence: Golexanolone Demonstrates Safety and Efficacy Signals

Safety: **Safe and well tolerated** in ~150 subjects across multiple studies. Oral compound **that passes the blood-brain barrier.**

Efficacy: **Consistent signs of efficacy** on both subjective (sleep, fatigue) and objective (EEG, CRT, SEV) measures.

Mechanism: **Acts as expected** by blocking excess GABA activity, decrease neuroinflammation and improving brain function.

Primary Biliary Cholangitis with Fatigue and Cognitive impairment — A Clear Orphan Entry Point

- **PBC is a rare autoimmune cholestatic liver disease**, affecting ~22/100,000, **90–95% women.**
- Beyond liver damage, **~60% report fatigue**, a major driver of poor quality of life .
- **Overall ~33%** of PBC patients have clinically significant **fatigue with cognitive impairment (Central fatigue) .**
- **Current drugs (URSO, OCA, pipeline therapies) do not affect central fatigue.**
- **Golexanolone in PBC** offers an attractive entry point **as first and only drug candidate** addressing **GABA-A–mediated central fatigue,** in parallel with therapies that target disease progression.

Source: 1.Jakub Gazda et al; Can J Gastroenterol Hepatol, Jun 19, 2021. 2. Phaw, N.A. Digestive Diseases and Sciences https://doi.org/10.1007/s10620-020-06502-0, May 2020 3.Laura Jopson, David EJ Jones; Dig Dis 2015:33 Suppl 2:109-14. Eirini I. Rigopoulou et al.; J Transl Int Med, Sep 2, 2023.

Ongoing Phase 1b/2a Study in PBC: UCAB-CT-05

Part A (Complete)

Placebo twice daily *(n=2)*

40 mg twice daily *(n=6)*

PK & Safety Review

- Safety, tolerability and pharmacokinetics of 40 mg BID in PBC patients.
- Investigate potential differences in metabolism of golexanolone.

- Safety review completed; no negative safety signals.
- No dose adjustments needed.

Completed

Part B (Ongoing)

Randomisation 1:1:1

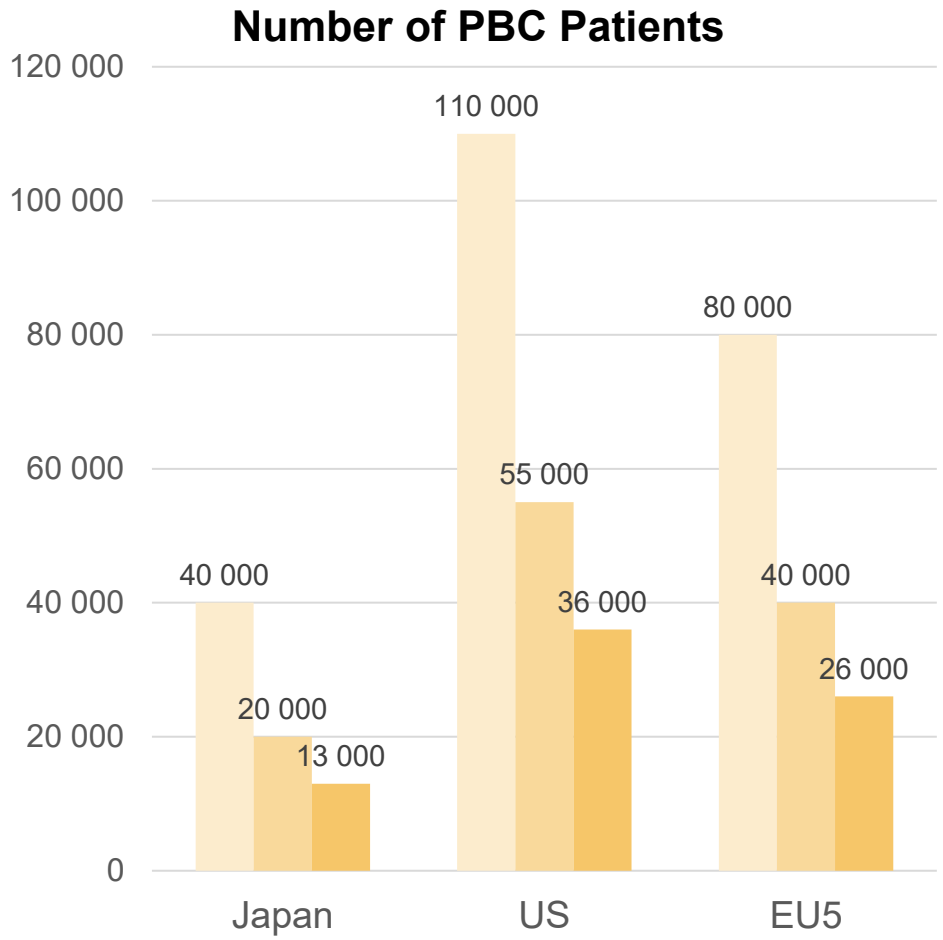
- Placebo twice daily (n=28*)
- 40 mg twice daily (n=28*)
- 80 mg twice daily (n=28*)

- Placebo-controlled, 40 & 80 mg vs placebo twice daily.
- PBC patients with clinically significant fatigue & cognitive symptoms.
- Evaluating safety, tolerability & efficacy.

- Study active across 8 countries with over 30 active clinics.
- 84 patients targeted; patient recruitment ongoing.
- Expected read-out Q2 2026.

Ongoing

USD 2.8–4.0B Annual Sales Opportunity for Golexanolone in Initial PBC Target Population



Estimated diagnosed prevalent PBC cases, 2027

~ 50% of PBC patients experience either moderate or severe fatigue

~ 33% of PBC patients with significant fatigue and cognitive symptoms

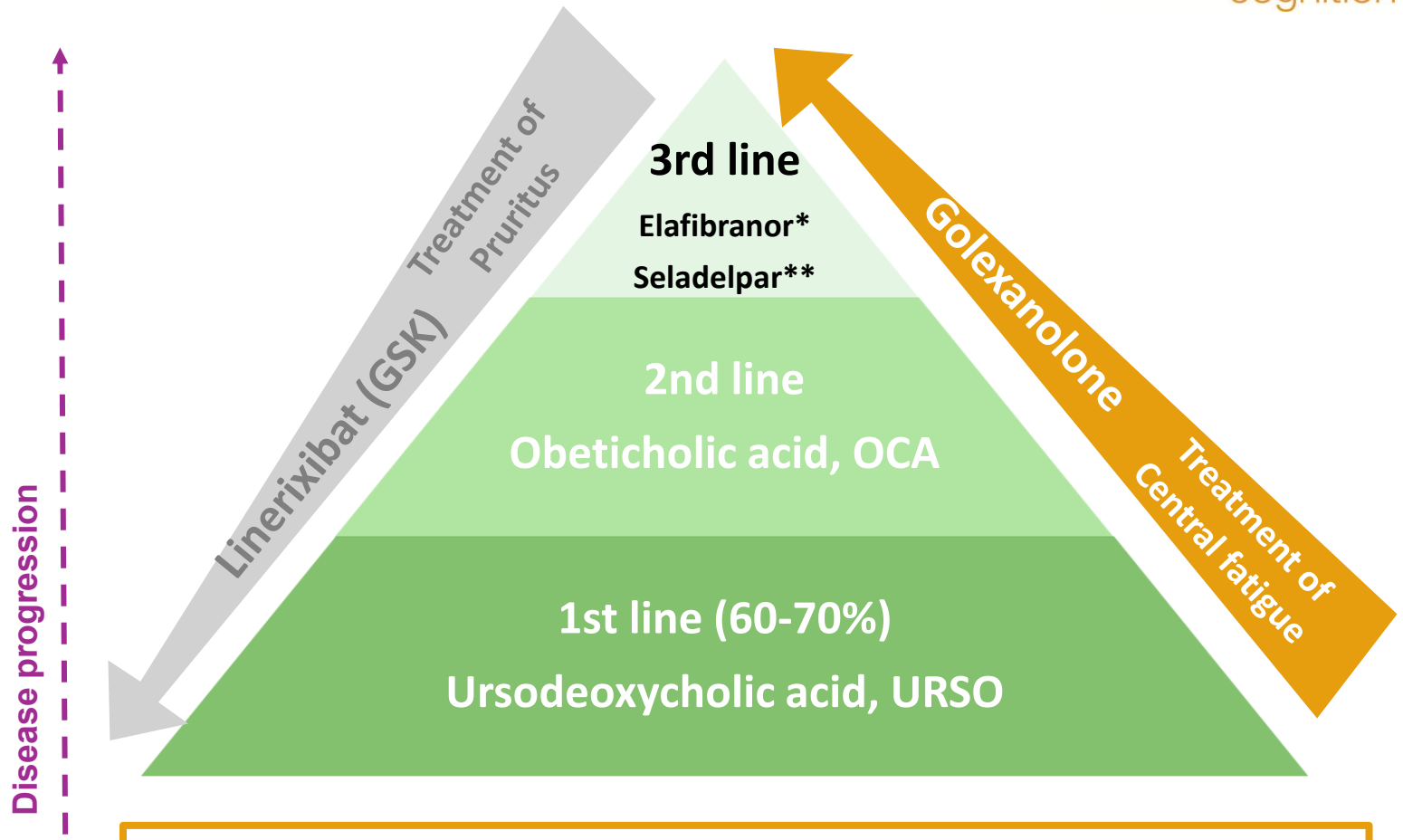
Annual Treatment price (per patient)
US: USD 55K to USD 80K
Japan & EU5 : USD 22K to USD 32K

USD 2.8 – 4B annual sales

Orphan drug designation granted in the US

Sources: 1. Global Data. Extracted Date: 18-Mar-2022.Eur5=UK, Germany, France, Spain, Italy (for Japan: Tanaka A., 2020. PBC: no longer a western Disease? Clin. Liver Dis., 16(6): 227-230. ; 2. Phaw NA, et al. Understanding Fatigue in Primary Biliary Cholangitis.Digestive diseases and sciences. 2020.; 3. Analysis conducted by Indegene/Medical Marketing Economics (MME) in December 2023.; 4. Wakix is the most relevant EDS benchmark given the adults only patient population at ~USD 95K (Nuplazid is a new benchmark in PD psychosis at ~USD 61K)

Golexanolone to be administered in parallel with treatment of underlying PBC, applicable through first to third line treatment modalities



Clinical Practice Guidelines: "The approach to **fatigue and its management needs to run in parallel with the management of the underlying disease** process, as is the case for pruritus, with a structured approach to management, quantifying fatigue and its impacts through the use of tools such as the PBC-40 QoL measure[2]"

Sources: IPSEN/Genfit – Iqirvo approved 10 June, 2024; ** Gilead/Cymabay.; Personal communictaion world leading KOL.; Hirschfelt et al., EASL Clinical Practice Guidelines: The diagnosis and management of patients with primary biliary cholangitis, 2017. J. of Hepatol. 67:145–172

Large Players Are Betting on PBC, and Golexanolone Offers Attractive Synergy Opportunities

Umecrine cognition

Acquired seladelpar (Livdelzi®), Phase 3/near approval in PBC

USD 4.3B
In total deal value

Acquired in 2024

Acquired Ocaliva®, marketed 2nd line PBC treatment

USD 1.0B
In total deal value

Acquired in 2023

Acquired rare liver disease / PBC portfolio, Phase 3 & earlier

USD 952M + CVR 226M
In total deal value

Acquired in 2023

Acquired elafibranor, Phase 3 PBC

EUR 480M + royalties
In total deal value

Acquired in 2022

Acquired mesdopetam (PD LID), Post Phase 2a / Phase 2b ongoing

USD 335M
In total deal value

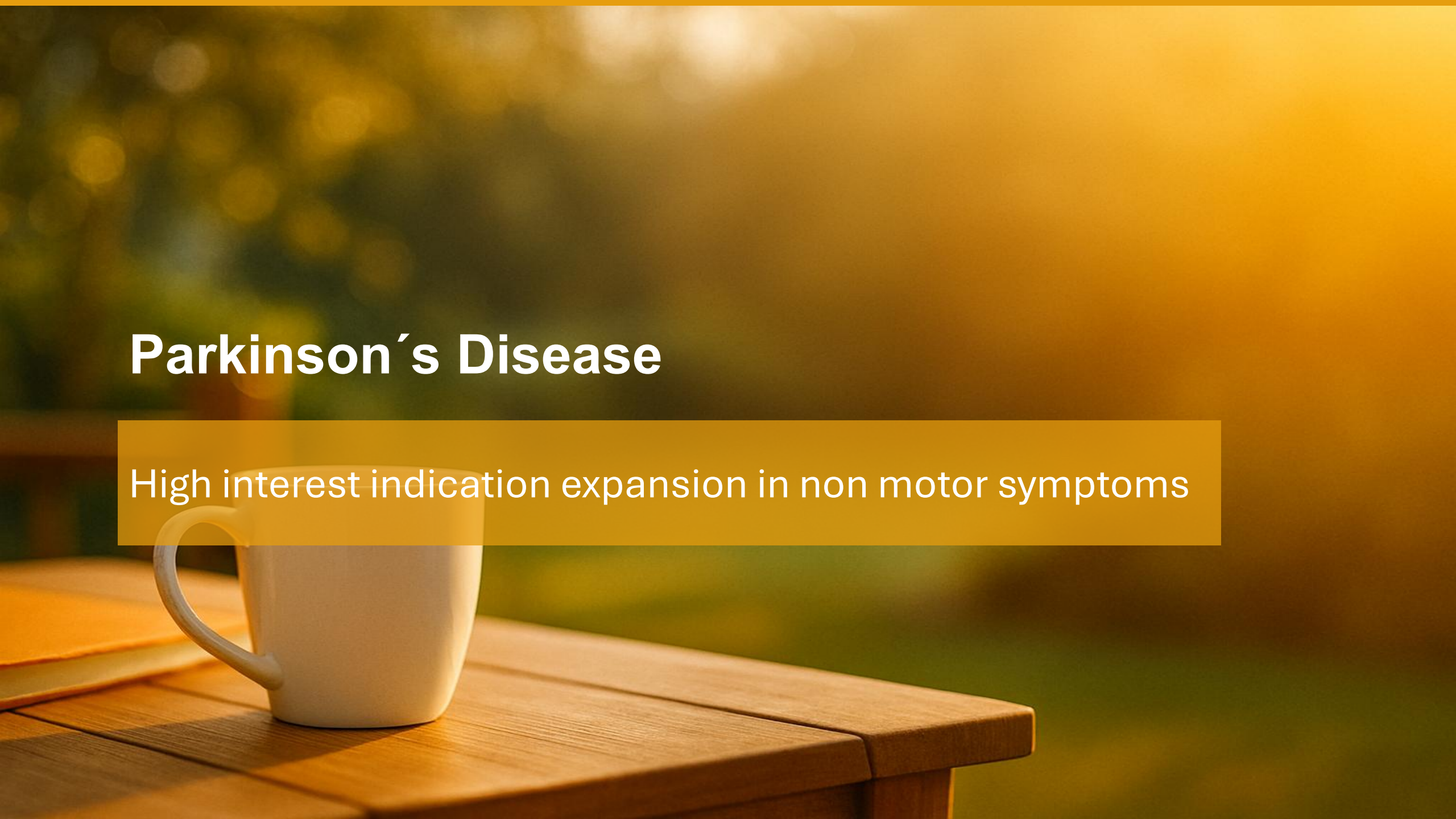
Acquired in 2021

Acquired zuranolone, neurosteroid / GABA modulator

USD 3.0B
In total deal value

Acquired in 2020

Symptom relief like itch and fatigue has become a top priority for PBC buyers



Parkinson´s Disease

High interest indication expansion in non motor symptoms

Expansion Opportunity in Parkinson´s Disease

Current disease management is symptomatic and limited

- Dominated by **dopaminergic augmentation** (e.g., Levodopa).
- Motor and non-motor symptom control remains suboptimal, often limited by side effects.
- No approved therapies that **slow or alter disease progression**.

Need for disease modifying treatments and non motor symptom relief

- **Disease-modifying** therapies remain a **major gap.**
- **Non-motor** symptoms such as Excessive Daytime Sleepiness (EDS), cognitive decline, fatigue, and anxiety **remain largely untreated**.
- Regulators recognize ESS and MWT as valid **registrational endpoints for EDS**.
- Disease modifying and non-motor symptoms represents a **large clinical and commercial whitespace** beyond motor-symptom drugs.
- Umecrine Cognition is currently the only company addressing **GABA-A–mediated fatigue and cognitive disorders in Parkinson's disease.**

Scientific and commercial interest for α-synuclein and neuroinflammation

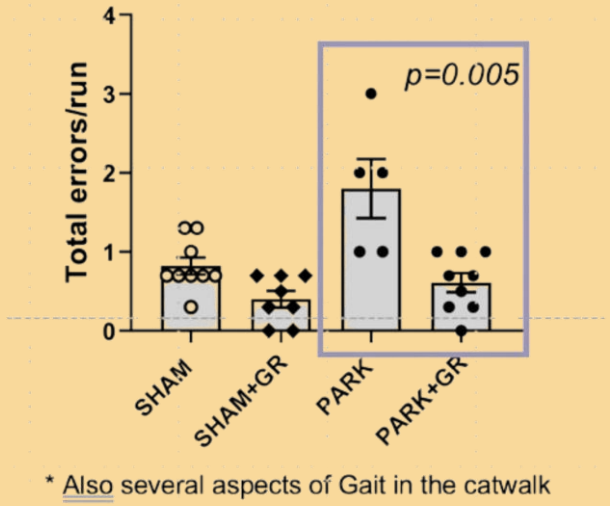
- Dual-targeting strategies (α-syn reduction + microglial modulation) are viewed as the **most promising path for true disease modification.**
- Novartis–Arrowhead RNAi **deal worth up to USD 2.2B (USD 200M upfront) highlights commercial heat around α-syn targets.**
- **Neuroinflammation, particularly microglia** modulation and glial-immune crosstalk**, is the rising star in PD drug discovery.**
- Growing industry focus driven by demand for therapies addressing **disease progression and non-motor outcomes.**

- **~2.6 million PD patients across 7MM markets.**
- **Global PD market USD 4.3b (2022) → projected USD 11.5b (2029).**
- **Growing focus on α-synuclein and neuroinflammation as dual disease drivers.**

Golexanolone Restores Motor and Cognitive Function Without Dopaminergic Side Effects

Umecrine cognition

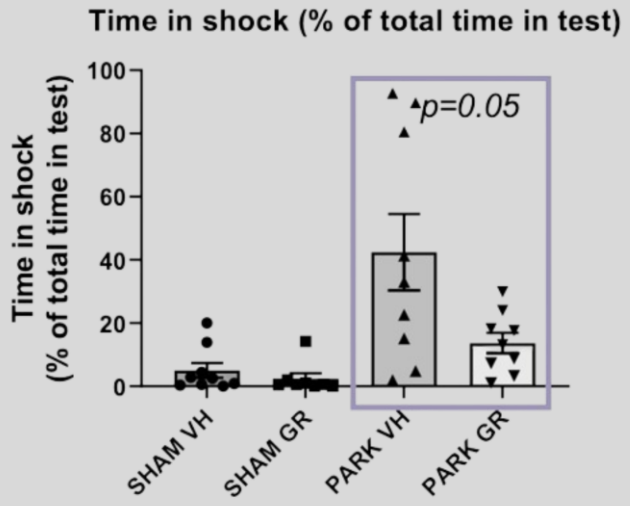
Motor coordination*



* Also several aspects of Gait in the catwalk

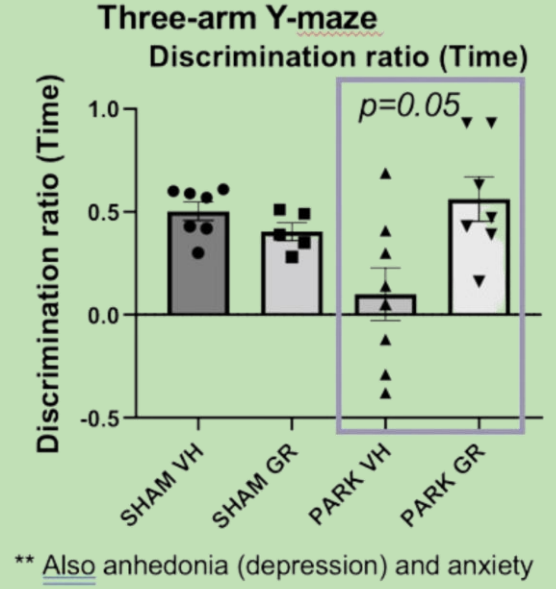
- **Decrease in total errors per run (p = 0.005).**
- Improved gait and coordination.
- Performance close to sham (normal) animals.

Fatigue



- **Decrease in time spent in shock (p = 0.05).**
- Indicates improved stamina and lower fatigue.
- Suggests greater stress tolerance.

Short-term spacial memory**



** Also anhedonia (depression) and anxiety

- **Increase in discrimination ratio (p = 0.05).**
- Improved cognitive performance and memory.
- Also positive effects on mood (anhedonia and anxiety).

Golexanolone reverses both motor and non-motor symptoms without dopaminergic side effects

Source: Izquierdo-Altarejos *P. et al.* (2024). *Front. Aging Neurosci.* 16:1417938.

Sham VH: Control rats with vehicle;
Sham GR: Control rats with golexanolone;
BDL VH: BDL rats with vehicle;
BDL GR: BDL rats with golexanolone

Golexanolone Hits Both PD Drivers (Preclinical)

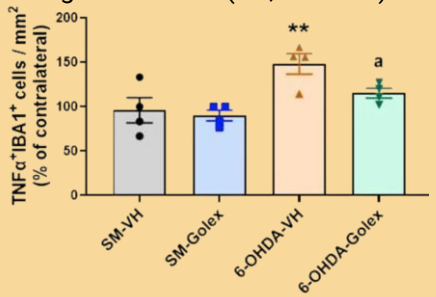
The microglia target – sustained improvement

- **Peer-reviewed PD model published in Frontiers in Immunology (2025).**
- Golexanolone reduced pro-inflammatory glial activation and cytokines in the 6-OHDA rat.

Inflammation and glia (6-OHDA rat, substantia nigra, 3–9 weeks)

- Microglial activation reduced; TNFα⁺/IBA1⁺ cells ≈ sham **(SN, 9 weeks; p = 0.006).**
- Pro-inflammatory cytokines reduced: TNFα and HMGB1 **(p≈0.03–0.05).**
- A1 astrocyte markers reduced: S100B **(p=0.024)** and vimentin **(p=0.0041).**
- **No dyskinesia observed in the model.**

TNFα⁺ microglia normalized by golexanolone (SN, 9 weeks)



* Significantly different from sham-operated rats
a Significantly different from Parkinson's rats
*, a: p < 0.05; ** p < 0.01; *** p< 0.0001

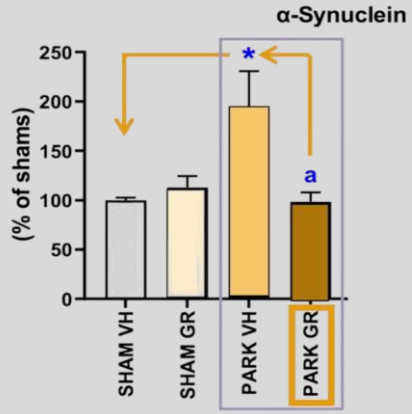
Mincheva et al., Frontiers in Immunology, 2025.

The α-Synuclein target – sustained improvement

- **Peer-reviewed PD model published in Front Aging Neuroscience (2024).**
- Golexanolone prevented the rise in alpha-synuclein and returned levels near sham.

α-Synuclein accumulation reduced

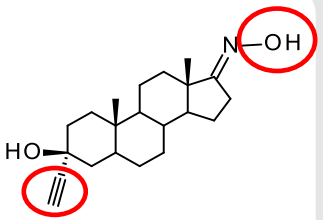
- **Vehicle PD ≈ 2.2× sham** (≈220% of normal α-synuclein).
- Golexanolone ≈ 1.0× sham (near baseline; vs vehicle **(p<0.05).**
- Interpretation: prevents the pathological increase in α-synuclein during treatment, consistent with disease-modification potential.



* Significantly different from sham-operated rats
a Significantly different from Parkinson's rats
*, a: p < 0.05; ** p < 0.01; *** p< 0.0001

Izquierdo-Altarejos et al., Frontiers in Aging Neurosciense, 2024

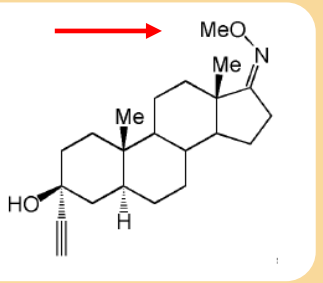
Analogue Candidates for Parkinson's Disease



GR3027/golexanolone

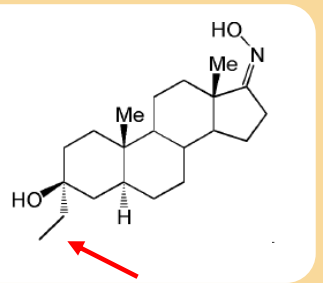
- WO 2008/063128.
- Granted in all territories (US, EPO, Asia, Australia…).
- Vast ADME/PK data in humans in vivo (Phase 2 study ongoing).
- Clinical data in HE; preclinical data in HE, PBC, PD.

Focus PBC



GR3053 (NCE)

- WO 2023/083978 (US; EPO; Canada; China).
- National filing phase.
- Partial receptor pharmacology data (GAMSA).
- In-silico prediction supports GR3053 likely to possess.
- adequate ADME/PK in humans in vivo similar to GR3027.



GR3055 (NCE)

- WO 2023/083978 (US; EPO; Canada; China.
- National filing phase.
- Partial receptor pharmacology data (GAMSA).
- In-silico prediction supports GR3055 likely to possess adequate ADME/PK in humans in vivo similar to GR3027.

Analogue candidates for Parkinson's disease and potentially other CNS disorders

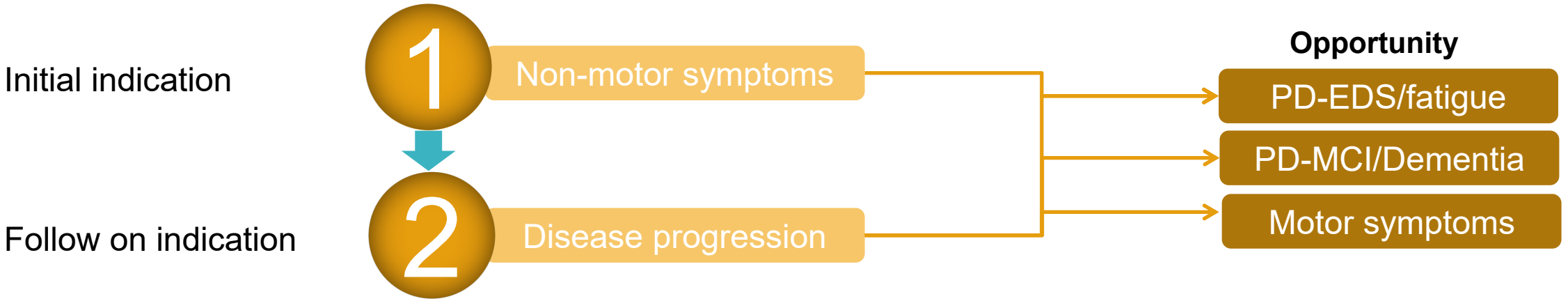
Go-to-Market Strategy - Shortest Way to Market Is by Starting in Non-Motor Symptoms

Initial indication in non motor symptoms

- **Non-motor symptoms in Parkinson's disease**, such as excessive daytime sleepiness and cognitive decline, provide a **de-risked and fast-to-approve entry point** with **validated regulatory endpoints** and limited competition.
- **Golexanolone** has already **demonstrated statistically significant effects** on both sleep and cognition in previous clinical studies, and **similar effects are expected for its analogues.**
- This indication allows **short and cost-efficient studies** supported by **regulatory precedent** for symptomatic treatments, with typical timelines of **six to twelve months** for symptomatic studies and **three to five years** for disease-modifying programs.

Scalable path beyond first approval

- The same mechanism supports expansion into **disease progression and motor symptoms.**
- Once efficacy is established in non-motor PD, the program can broaden to address underlying neuroinflammation and α-synuclein–related pathology, **targeting disease modification.**
- **This enables** lifecycle growth and alignment with EMA/FDA guidance for therapies addressing **both symptomatic and disease-modifying outcomes in Parkinson's.**



Competitive Landscape in Parkinson's Disease — Alone in Targeting GABA-A and Neuroinflammation

Big Pharma

Roche
Has several α-synuclein–targeting antibodies (e.g., prasinezumab, partnered with Prothena) and neuroinflammation efforts in Parkinson's.

DENALI THERAPEUTICS
Runs LRRK2 inhibitor programs (e.g., DNL151, DNL201) specifically for Parkinson's disease, including genetically driven cases.

NOVARTIS
Collaborates on RNA-based α-synuclein–lowering therapies through partnerships such as with Arrowhead RNAi (the USD 2.2B deal).

AstraZeneca
Has neuroinflammation and microglia-focused programs within its neurodegeneration pipeline, with relevance to Parkinson's pathology.

GABA-A and Neuroinflammation (Umecrine Cognition)

- **Only company with an active program targeting GABA-A–mediated central fatigue in Parkinson's disease.**
- **Unique, first-in-class neurosteroid antagonist mechanism** distinct from dopaminergic and α-synuclein approaches.
- **Addresses major unmet non-motor symptoms** such as fatigue, cognitive decline, and sleep dysfunction with **validated EDS endpoints.**
- **Demonstrated preclinical efficacy** reversing both motor and non-motor symptoms without inducing dyskinesia.
- **Strong translational foundation** with extensive human ADME/PK data and an ongoing Phase 2 program in PBC with golexanolone.
- **Parkinson's program builds on next-generation analogs** optimized for CNS exposure and sustained GABA-A modulation.

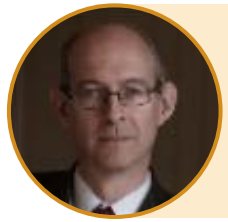
Strong leadership team with extensive industry experience

Viktor Drvota, (MD, PhD)
Chief Executive Officer
23 years in life science VC. Former Associate Professor and consultant at Karolinska. Broad experience in preclinical and clinical research.

Pernilla Sandwall (MSc)
Chief Operating Officer
30+ years industry experience in clinical development across global and SME pharma companies.

Magnus Doverskog, CSO (MSc PhD MBA)
SVP & Chief Scientific Officer
25 years of industry drug discovery and development. Senior roles at Astra Pain Control, Biovitrum, IMED. Former CEO of Umecrine Cognition. Affiliated to Department of Neuroscience at Karolinska.

Roberto Camerini, (MD, PhD)
Medical Director
35 years in industry with executive Clinical R&D roles at Abbott, Serono, Sigma-Tau, Alfasigma, Cosmo, Reithera, Epigen.



Hans Cristopher Toll, CFO (MSc. Economics)
Chief Financial Officer
25+ years international experience as CFO and business controller.

Board of Directors

Anders Bladh, BSBA – Chairman
10 years at Handelsbanken, entrepreneur, including setting up and running Intervalor, a leading Nordic company in marketing financial products. Owner of Ribbskottet AB.

Bruce Scharschmidt , MD – Director
Previously Sr. VP/Chief Medical & Development Officer at Hyperion Therapeutics. Past President of American Society of Clinical Investigation.

Thomas Blackburn PHD, Dsc. – Director
40+ years experience within pharma and biotech with C-level and senior mgmt. positions at major pharma-ceuticals (ICI, Becham/-SmithKline,Beecham) and US biotechs.

Torbjörn Bäckström MD, PhD - Director & Co-founder
Professor at the Department of Clinical Science, Obstetrics and Gynecology Umeå University, Head of the Umeå Neurosteroid Research Center.

John Öhd MD, PhD – Director
Long experience in leadership roles within R&D of AstraZeneca, Shire Pharmaceuticals, and Medivir. CSO at Karolinska Development.

Umecrine Cognition is seeking 7 MEUR

Umecrine Cognition poses a substantially de-risked, late-stage investment opportunity
built on a modulating steroid antagonist with unique properties:

Close to key inflection point: ongoing phase 2 study in PBC expected to be fully recruited in 2026
Positive results are likely to trigger partnering opportunities.

Strong deal activity in orphan and rare liver diseases creating an attractive and potential near term exit in PBC.

Additional upside from the PD program supported by peer-reviewed data and MJFF validation within a high interest area.

Use of proceeds:

- **Complete PBC Phase 2** and prepare for partnering and next-phase readiness.
- **Advance new** compounds toward IND-enabling and maintain spin-out optionality.

Umecrine cognition

Fighting central fatigue and cognitive impairment caused by neuroinflammation with golexanolone, a novel small molecule GABA-A receptor-modulating steroid antagonist

Viktor.Drvota@umecrine.se
www.umecrinecognition.com