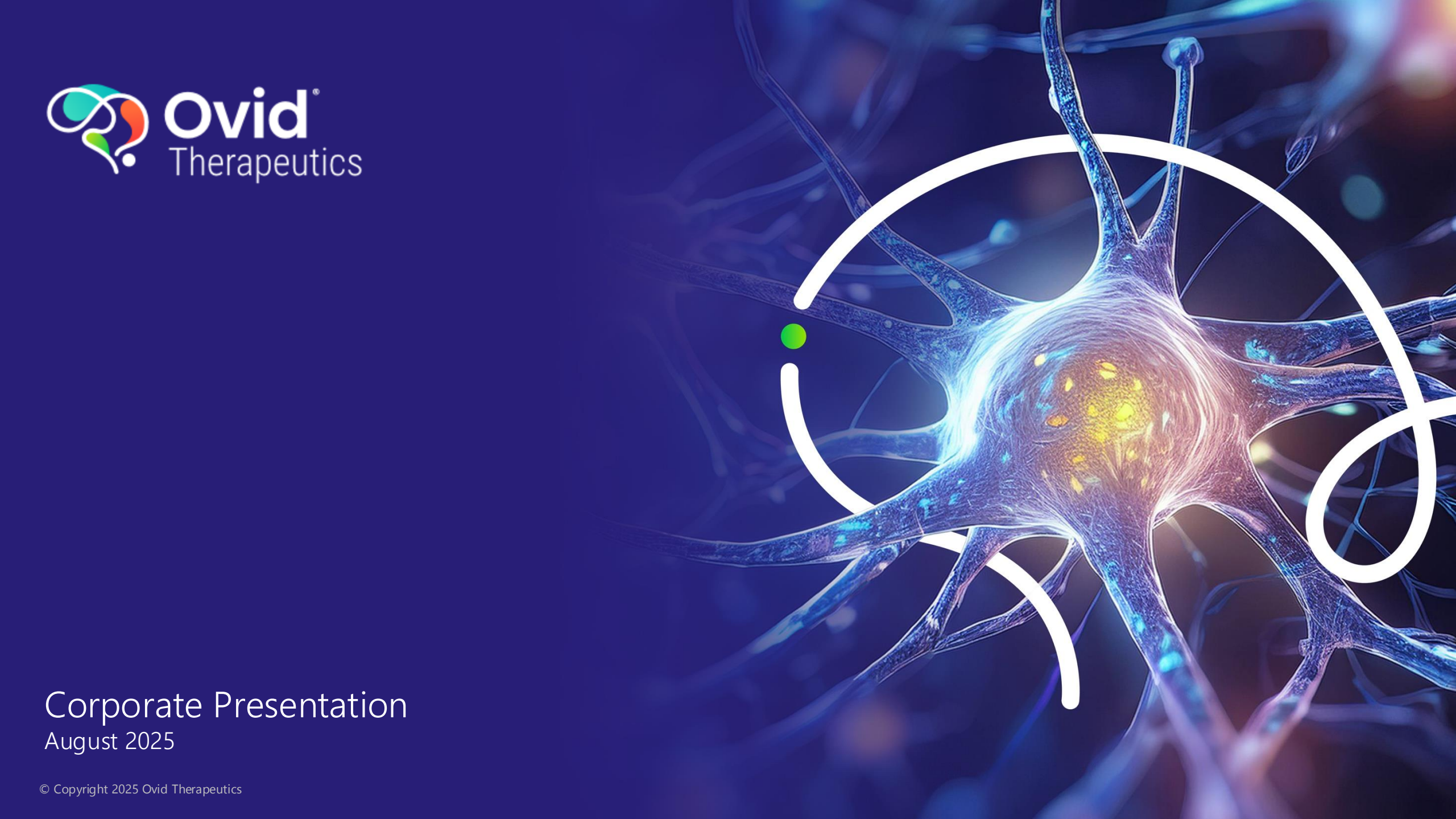
Ovid Therapeutics



Corporate Presentation

August 2025

© Copyright 2025 Ovid Therapeutics

Forward looking statements

This presentation contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995 including, without limitation, the potential therapeutic benefits of Ovid's current or future product candidates and pipeline programs; Ovid's expectations regarding the duration of its cash balance, and the expectation that it will support the advancement of Ovid's operations and development program; statements regarding the expected timing of the initiation, completion, and results and data of Ovid's clinical studies; expected timing of IND submission for OV4041 oral; the outcome of Ovid's evaluation of the results of recently completed competitor trials and its impact to the OV888/GV101 program; expectations regarding patent term extension for OV329; the potential use, development and therapeutic opportunity of OV329, OV350 and other compounds from Ovid's library of direct activators of KCC2; the likelihood that data, including safety and tolerability data, for OV329 will support future development and therapeutic potential; the suitability of OV329 for a range of indication opportunities; the clinical and regulatory development of the KCC2 compounds in Ovid's library, including OV350 IV and OV4071 oral; the suitability of Ovid's library of novel, direct KCC2 transporter activators for a range of formulations and administrations; and expectations regarding the size of the market for Ovid's current or future product candidates and pipeline programs. You can identify forward-looking statements because they contain words such as "will," "may," "plan," "believes," "intends," "anticipates," "design," "advance," "target," "seek," "expects," "demonstrates," and "potential," and similar expressions (as well as other words or expressions referencing future events, conditions or circumstances).

Forward-looking statements are based on Ovid's current expectations and assumptions. Because forward-looking statements relate to the future, they are subject to inherent uncertainties, risks and changes in circumstances that may differ materially from those contemplated by the forward-looking statements, which are neither statements of historical factor guarantees or assurances of future performance. Important risks that could cause actual results to differ materially from those in the forward-looking statements include, without limitation: uncertainties inherent in the preclinical and clinical development and regulatory approval processes; whether interim or preliminary results from a clinical trial will be predictive of the final results of the trial or the results of future trials; the risk that Ovid may be unable to raise additional capital and could be forced to delay, further reduce or to explore other strategic options for certain of its development programs; the risk that Ovid may not be able to realize the intended benefits of its business strategy; Ovid's ability to identify business development targets or strategic partners, to enter into strategic transactions on favorable terms, or to consummate and realize the benefits of any business development transactions; Ovid's or any of its partners' abilities to meet anticipated deadlines and milestones; and/or unanticipated impacts or delays due to macroeconomic and geopolitical conditions. Additional risks that could cause actual results to differ materially from those in the forward-looking statements are set forth under the caption "Risk Factors" in Ovid's quarterly report on form 10-Q filed with the Securities and Exchange Commission (SEC) on August 13, 2025, and in future filings Ovid makes with the SEC. Any forward-looking statements contained in this presentation speak only as of the date hereof, and Ovid assumes no obligation to update any forward-looking statements contained herein, whether because of any new information, future events, changed circumstances or otherwise, except as otherwise required by law.

©2025 Ovid Therapeutics | All Rights Reserved

Medicines to quell conditions caused by neural hyperexcitability

Foundational biological targets

implicated in conditions driven by neural hyperexcitability and which have broad potential therapeutic utility

Pipeline of highly specific small molecules

intended to culminate in a fully integrated neurotherapeutics company with multiple clinical-stage programs and commercial medicines

Differentiated mechanisms of action

that stand out in a growing field of me-too medicines

Cash balance of $38.3 million

expected to fund operations into early second half of 2026[1]

1. As of June 30, 2025

©2025 Ovid Therapeutics | All Rights Reserved

Focused pipeline with multiple near-term milestones

Programs	Indication opportunities	Preclinical	Phase 1	Phase 2	Anticipated milestones*
GABA-aminotransferase inhibitor					
OV329	Drug resistant adult epilepsies (DREs) & developmental epileptic encephalopathies (DEEs)				Phase 1 topline Q3 2025 (includes safety and biomarkers of potential clinical effect) Phase 2a initiation Q1 2026; topline Q1 2027
KCC2 direct activator portfolio					
OV350 IV	First-in-human potential proof of mechanism				Phase 1 initiated Q1 2025 Safety, tolerability and PK Q4 2025
OV4071 oral	Psychosis assoc. with Parkinson's disease and Lewy body dementia				IND-enabling studies in progress Phase 1 initiation expected in Q2 2026 Patient Phase 1b initiation in Q3 2026; topline results in Q1 2027
OV4041 oral	Generalized anxiety disorder or Rett syndrome				Initiating IND-enabling late 2025 IND submission late H2 2026

* Subject to Ovid capital runway or partnerships.

©2025 Ovid Therapeutics | All Rights Reserved

OV329: A next-generation, potential best-in-class GABA-aminotransferase (AT) inhibitor

Precision inhibition of neuronal hyperexcitability, including drug-resistant epilepsies (DREs)

Validated mechanism for seizures, with differentiated safety from 1st generation

Clinical results
Phase 1 safety, tolerability and biomarkers Q3 2025; Phase 2 initiation Q1 2026

IP through 2041 (assumes five-year patent term extension)

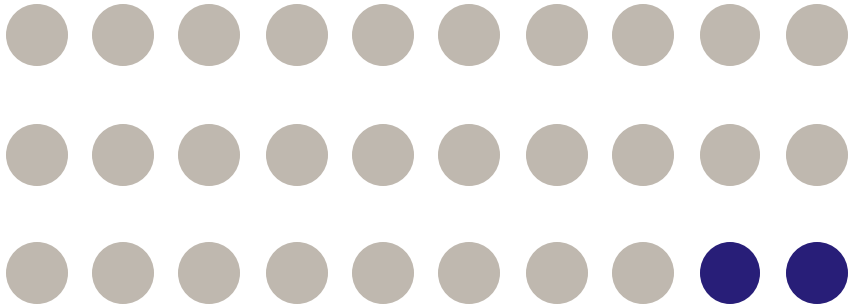
10 patent families

A potential medicine for people living with treatment-resistant focal seizures

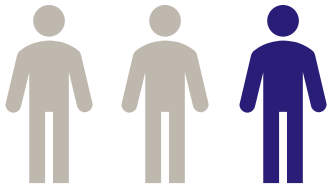
© Copyright 2025 Ovid Therapeutics

Drug-resistant epilepsy (DRE): A significant unmet need for a safe and well-tolerated GABA-AT inhibitor

30 anti-seizure medications approved in 15 years, but only 2 with novel mechanisms



A crowded treatment landscape and yet—
>1 in 3 patients live with uncontrolled seizures



47% of epilepsy patients in the U.S. report poly-pharmacy use taking on average five medications[1]



Each dot = 1 FDA-approved ASM; Purple dot= Fycompa and Cenobamate

1. Terman SW, Aubert CE, Hill CE, et al. Polypharmacy in patients with epilepsy: a nationally representative cross-sectional study. Epilepsy Behav. 2020;111:10726

© Copyright 2025 Ovid Therapeutics

Unmet need in drug-resistant epilepsies & OV329 opportunity

Challenges of existing GABA-enhancing medicines

- **Short-acting**
  - Inhibition not sustained
- **Sedating**
- **High dose burden** of 1st generation medicine
  - Sabril (vigabatrin) starting dose is 3 grams, OV329 is ~1000-fold LESS drug
- **Safety challenges of 1st generation**
  - Vigabatrin causes irreversible visual toxicity
  - Black Box and REMS
  - Routine ocular monitoring required

Intended OV329 target product profile*

Optimally tuned inhibition at low doses

- Durable inhibition and anti-convulsant activity

Sustained seizure reduction

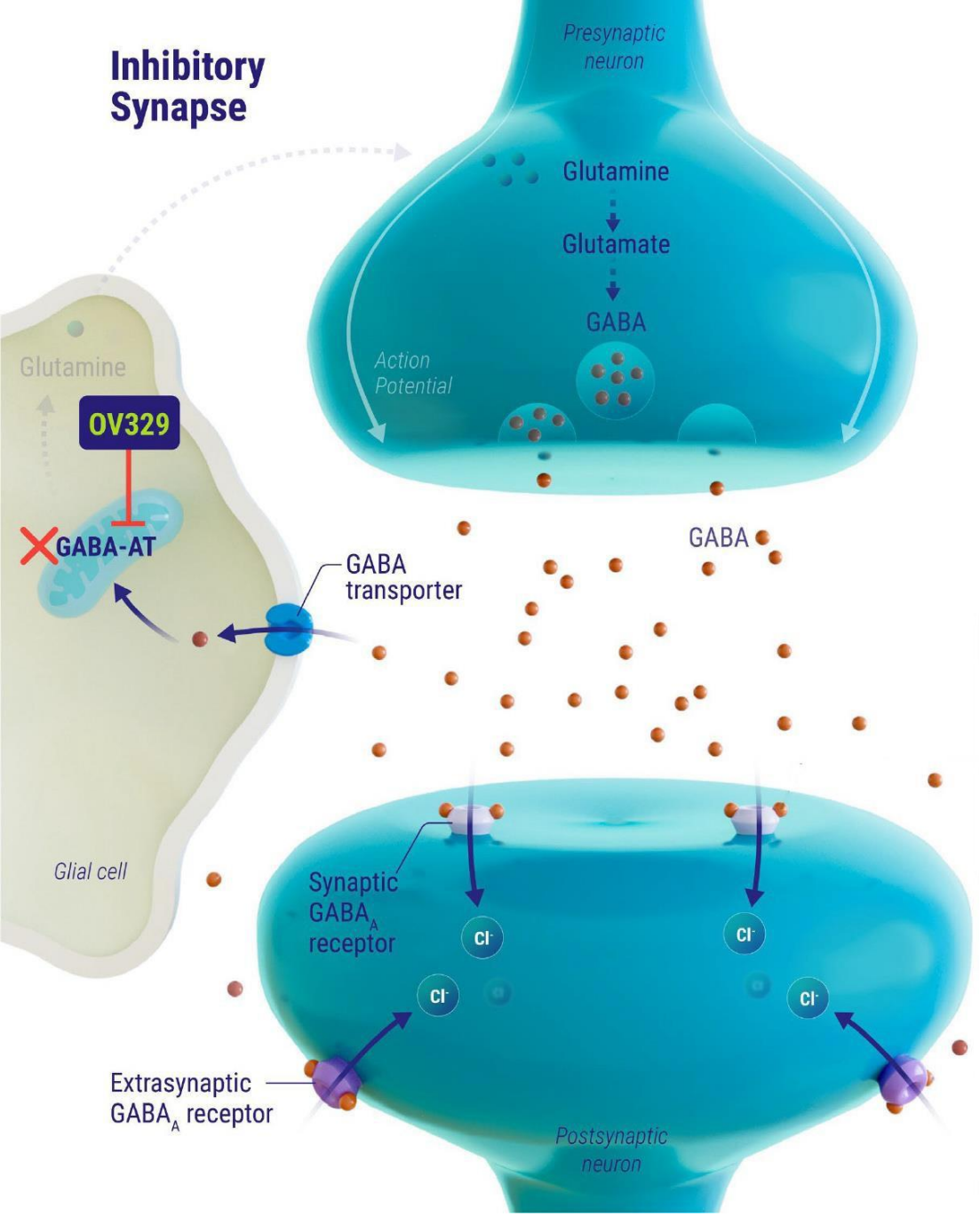
- Strong reduction across focal & other seizure types

Improved safety profile

- No evidence of ocular changes in humans
- No monitoring requirement expected on label
- No expected titration
- Not sedating in humans
- No anticipated drug-drug interactions

*Intended label reflected; profile will need to be demonstrated through future clinical development and patient studies

©2025 Ovid Therapeutics | All Rights Reserved



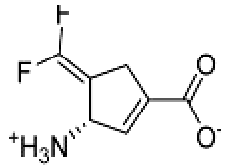
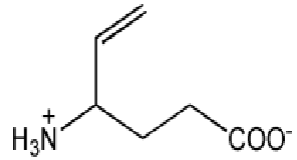
Mechanism of action

- Validated mechanism of action
- Inhibits GABA-AT, the enzyme that catabolizes the inhibitory neurotransmitter, GABA
- Increases GABA in the synapse & extrasynaptic regions
- Believed to optimally tune GABA to create an inhibitory neural milieu

Silverman RB. Chem Rev. 2018 Apr 11;118(7):4037-4070. doi: 10.1021/acs.chemrev.8b00009. Epub 2018 Mar 23. PMID: 29569907; PMCID: PMC8459698
Colmers P et al. eNeuro 27 June 2024, 11 (7) ENEURO.0137-24.2024; https://doi.org/10.1523/ENEURO.0137-24.2024

©2025 Ovid Therapeutics | All Rights Reserved

Rationally designed to deliver potential best-in-class profile

	OV329	Vigabatrin
Molecule		
Potency (IC_{50})[1]	1,000-fold more potent (~0.1 - 0.3 mM) [1]	~60 – 100 mM
Exposure	$T_{1/2}$ ~1.0 Hour while delivering prolonged enzyme suppression[2]	$T_{1/2}$ >5.0 Hours
Mechanism of enzyme inhibition	Electrostatic (irreversible) (Primarily enamine pathway)[3]	Covalent modification of GABA-AT (irreversible)
Therapeutic index[4,5]	✓ No ocular changes in humans	✗ Visual toxicity at therapeutic dose
Inhibition delivered	Phasic & tonic inhibition (Increases GABA in synapse & extrasynaptic region)	Toxicity limits ability to achieve phasic & tonic inhibition

1. J Med Chem. 2012 Jan 26; 55(2): 567–575; 2. J Am Chem Soc. 2018 Feb 14; 140(6): 2151–2164
2. Ovid data on file.
3. Feja et al. OV329, a novel highly potent γ-aminobutyric acid aminotransferase inactivator, induces pronounced anticonvulsant effects in the pentylenetetrazol seizure threshold test and in amygdala-kindled rats. Epilepsia. 2021 Dec;62(12):3091-3104. doi:10.1111/epi.17090. Epub 2021 Oct 7.
3. As seen in clinical trials to date.
Ovid data on file. Therapeutic index measured in Sprague Dawley rats, a proxy model used to assess ocular safety.

©2025 Ovid Therapeutics | All Rights Reserved

OV329 has differentiated PK, PD & ocular profile in preclinical findings

- ✓ Penetrates the brain, as it is found in animal plasma and brain tissues[1]
- ✓ Anti-convulsant activity across an extensive range of seizure models
- ✓ >100-1,000x more potent than vigabatrin in animal and in-vitro studies[1]
- ✓ Undetectable in the retina, eye and brain tissue (vigabatrin shown to accumulate 4x in the retina)[2]
- ✓ Rapid tissue clearance properties and half-life (1.5 hours) compared to vigabatrin (4 hours)[1]
- ✓ Established therapeutic index; vigabatrin produces ocular toxicity at therapeutic dose

1. Mukherjee, J., et al. (2023). Blocking of GABA-AT Activity Selectively Alters Tonic and Phasic Inhibition. Poster presented at the 2023 American Epilepsy Society Conference
2. Tsai, J., et al. (2024). Evaluation of the Potential Accumulation of OV329 in the Brain, Retina, and Eye Following Continuous Infusion. Poster presented at the 2024 Epilepsy Pipeline Conference

©2025 Ovid Therapeutics | All Rights Reserved

Anti-convulsant activity demonstrated in 9 seizure models

Seizure reduction seen in chronic & acute seizure models

	i.v. (ivPTZ)	NMDA-Induced Infantile Spasm model	Audiogenic Seizure	Amygdala Kindled	Corneal Kindled	Intrahippocampal Kainate Model of Mesial-Temporal Lobe Epilepsy (MTLE)	Intraamygdala Kainate Model of Mesial-Temporal Lobe Epilepsy (MTLE)	Lithium-Pilocarpine	Dravet *Scn1a* $^{A1783V/WT}$
Injury Model	Acute/ seizure	Acute/ seizure	Acute	Chronic/ epilepsy	Chronic/ epilepsy	Chronic/ epilepsy	Epilepsy prevention/ modification	Acute/ seizure	Chronic/ Genetic epilepsy
Clinical Correlate	Nonconvulsive Seizures (e.g., absence, myoclonic)	Infantile spasms	Generalized seizures	Chronic focal to bilateral tonic-clonic seizure/ Pharmacoresistant seizures	Chronic focal to bilateral tonic-clonic seizure	Focal Mesial temporal lobe epilepsy/ Pharmacoresistant seizures; Status Epilepticus	Focal Mesial temporal lobe epilepsy/ Pharmacoresistant seizures; Status Epilepticus	Like human, rodents exhibit EEG abnormalities, convulsions, and cognitive impairment	Spontaneous seizures, higher rate of SUDEP. Hyperthermia-induced Pharmcoresistant seizures.
Species	Rat	Mouse	Mouse	Rat	Mouse	Mouse	Mouse	Rat	Mouse
Dosing	Acute (5, 20, 40 mg/kg i.p.)	Acute (0.0025, 0.01, 0.1, 1 mg/kg, p.o.)	Acute (0.01, 0.05, 0.1 mg/kg, p.o.)	Acute (30, 40 mg/kg, i.p.)	Acute (1, 3, 10, 20, 30, 40, 60 mg/kg, p.o.)	Acute, single dose (0.01, 0.1, 1, 10 mg/kg, p.o.; 10 mg/kg, i.p.) Subacute (8 days q.d.) 0.3, 1.0 and 3.0 mg/kg/day (p.o.)	Acute (40 mg/kg p.o.)	Acute (15mg/kg, IV)	Repeat (10mg/kg x 4d, IP)
Activity	+	+	+	+	+	+	+	+	+

Ovid data on file

©2025 Ovid Therapeutics | All Rights Reserved

Differentiated safety in retinal model required by regulators

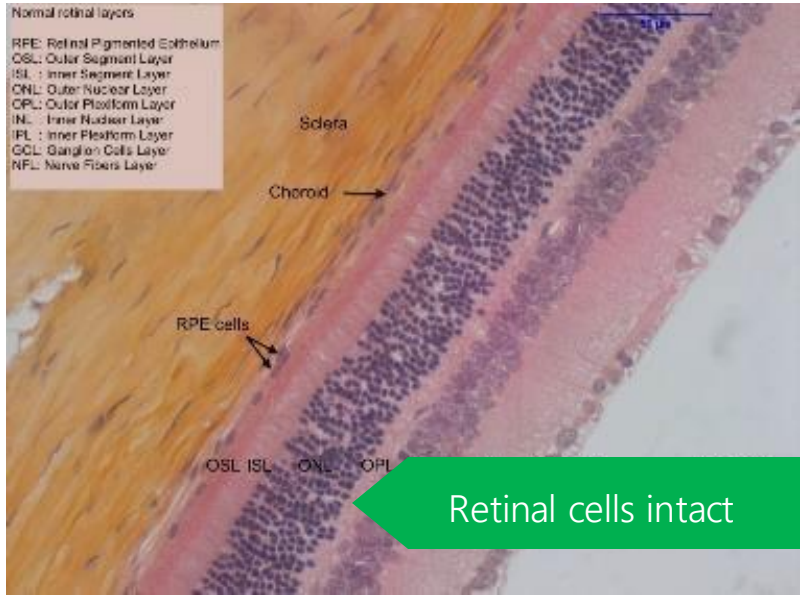
Anti-convulsant activity in 9 animal seizure models

- Represent a wide range of seizures
- Clinically active at low doses

Ocular safety profile differentiation

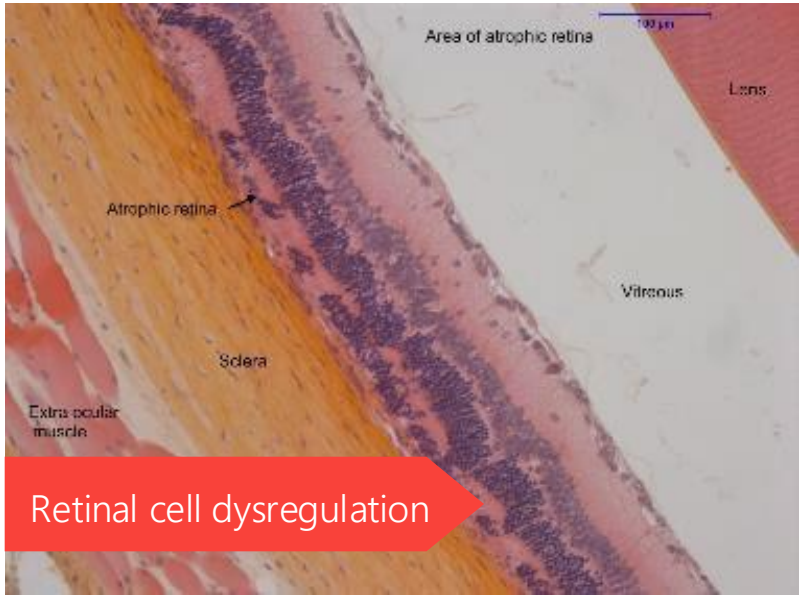
- Demonstrated in 2 models & toxicology
- Unique potency, binding & clearance profile likely related to lack of accumulation in eye

OV329 3.0 mg/kg
(Therapeutic dose)



No ocular effects seen in 3 mg/kg q.d. in rats

vigabatrin 300 mg/kg
(Therapeutic dose)



Ocular changes in more than half of rats treated (300 mg/kg)

45-day study

Ovid data on file

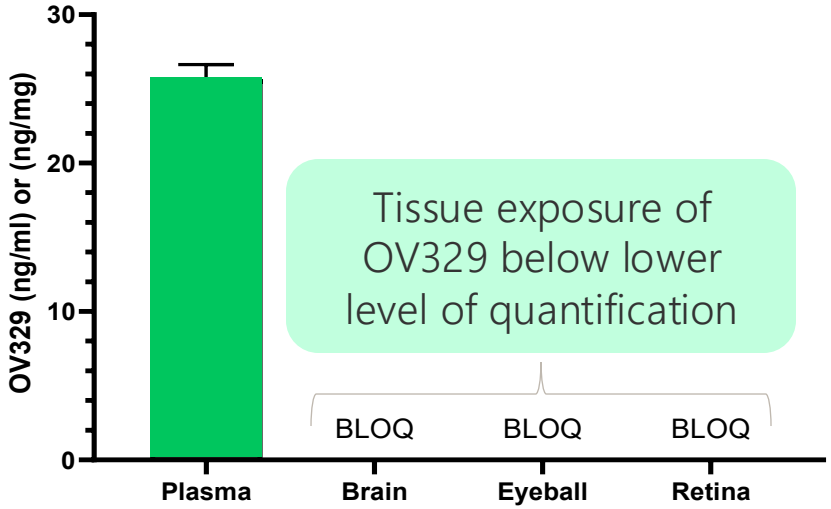
©2025 Ovid Therapeutics | All Rights Reserved

Head-to-head ocular accumulation study of OV329 versus vigabatrin

Lack of retinal accumulation of OV329 supports differentiated ocular safety profile vs. vigabatrin[1]

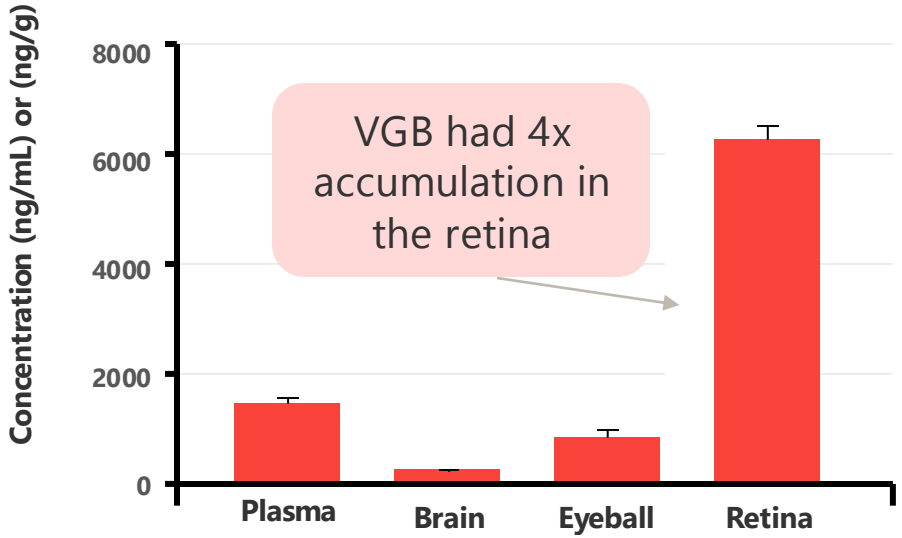
OV329

Mean Plasma and Tissue Concentration 5.0 mg/kg/day



VIGABATRIN

Mean Plasma and Tissue Concentration at 80.0 mg/kg/day



FINDINGS[1]

- OV329 penetrated the brain, was present in the plasma and then cleared the tissue
- No accumulation detected of OV329 in the eye or retina
- 4x greater exposure of vigabatrin in retina as compared to plasma
- Suggests vigabatrin, but not OV329, preferentially partitions into the retina when plasma exposure is kept at a relatively constant level

1. Tsai, J., et al. (2024). OV329 A potent GABA-AT inhibitor Does Not Accumulate in Mouse Retina A Pharmacokinetic Study to Differentiate Eye Accumulation between Vigabatrin Poster presented at the 2024 American Epilepsy Society

©2025 Ovid Therapeutics | All Rights Reserved

OV329 Phase 1 trial objectives

Exploratory biomarkers measure biological effect

- Magnetic resonance spectroscopy (MRS)
- Transcranial magnetic stimulation (TMS)
- Electroencephalography (EEG)

Other endpoints

- Pharmacokinetics
- Safety and tolerability
- Ophthalmic safety metrics & monitoring
  - Best corrected visual acuity
  - Fundus photography
  - Indirect dilated ophthalmoscopy
  - Automated threshold visual field perimetry
  - Optical coherence tomography (OCT)

Excellent safety observed to date

- No serious adverse events
- No treatment- related adverse events

Current cohort

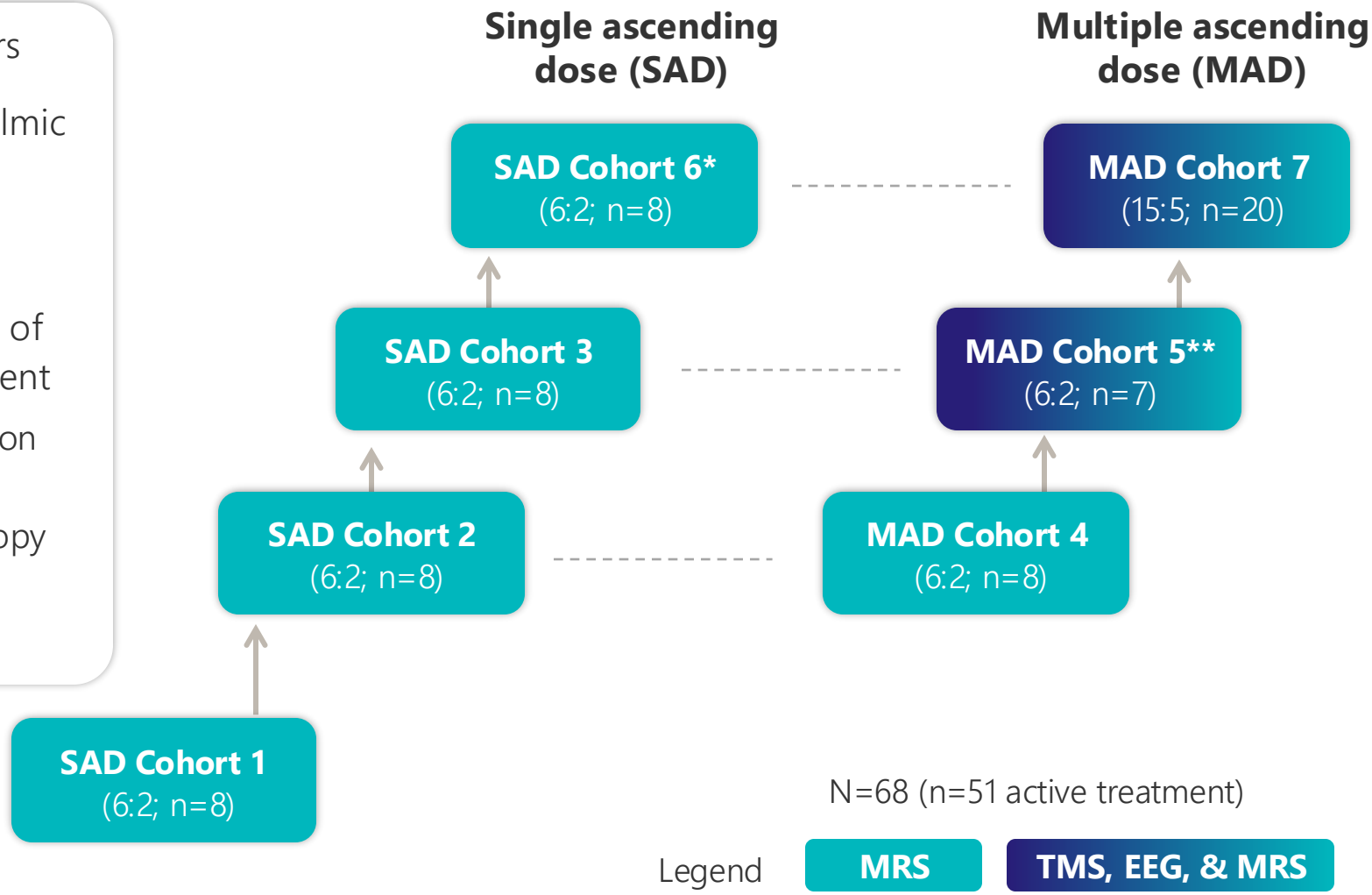
- High dose cohort added to optimize Phase 2 dosing opportunities

GOAL: Establish pharmacodynamic activity, safety & tolerability

©2025 Ovid Therapeutics | All Rights Reserved

OV329 Phase 1 trial design:

- Ph 1 SAD/MAD in healthy volunteers
- Safety/tolerability including ophthalmic safety & metrics
- Pharmacokinetics
- Exploratory biomarker assessments of biological effect & target engagement
  - Transcranial magnetic stimulation (TMS)
  - Magnetic resonance spectroscopy (MRS)
  - Electroencephalography (EEG)



*no imaging
**one person withdrew due to a family matter

©2025 Ovid Therapeutics | All Rights Reserved

Biomarker strategy applied in Phase 1

- Healthy volunteers measured pre- and post-treatment with OV329, includes placebo comparators
- Multiple parameters being assessed via:
  - Magnetic resonance spectroscopy
  - Transcranial magnetic stimulation
  - Electroencephalogram
- Leverage biomarker parameters that have measured vigabatrin & other GABAergic ASMs
- Assess drug effect after 7 days of treatment, relative to participant baselines and placebo
- Designed to detect directional signal
- Good safety and tolerability profile with no drug-related ocular changes

©2025 Ovid Therapeutics | All Rights Reserved

Comprehensive biomarkers to evaluate OV329

Tool	Magnetic resonance spectroscopy (MRS)	Transcranial magnetic stimulation (TMS)	Electroencephalogram (EEG)
Measures	**Neurotransmitter concentrations**	**Cortical excitability and brain circuit function**	**Brain waves linked to inhibitory (GABAergic) activity**
Metrics* (positive & negative controls)	• GABA concentrations in the medial parietal lobe	• Cortical silent period (CSP) • Paired-pulse long-interval intracortical inhibition (LICI) • Paired-pulse short-interval intracortical inhibition (SICI) • Resting motor threshold (rMT) • Intracortical facilitation (ICF)	High and low frequencies
What it suggests	✓ **Target engagement** as measured by increased in GABA concentrations using modern MRI "fitting" technology	✓ **Pharmacodynamic activity** on $GABA_A$, $GABA_B$ receptors and overall enhancing brain inhibition ✗ No excitatory (glutamatergic) activity	✓ **GABAergic pharmacodynamic** effect as shown by changes in high frequency brain activity

* All metrics compare post-OV329 values with baseline

©2025 Ovid Therapeutics | All Rights Reserved

Rationale for biomarkers & desired results

Measurement/Endpoint	Precedent	Desired result	What it may tell us
TMS Long-interval intracortical inhibition (LICI 150)	1st generation (VGB) showed increase	 Increase	Pharmacodynamic response consistent with increase in GABA
TMS CSP Duration	VGB showed prolongation	 Increase	Pharmacodynamic response consistent with increase in GABA
MRS GABA concentration	Multiple anti-seizure medicines have shown increase	 Increase	Measure of GABA increase could validate target engagement
EEG Brain wave frequency	GABAergic ASMs increase beta & gamma power	 Increase	Pharmacodynamic response consistent with increase in GABA

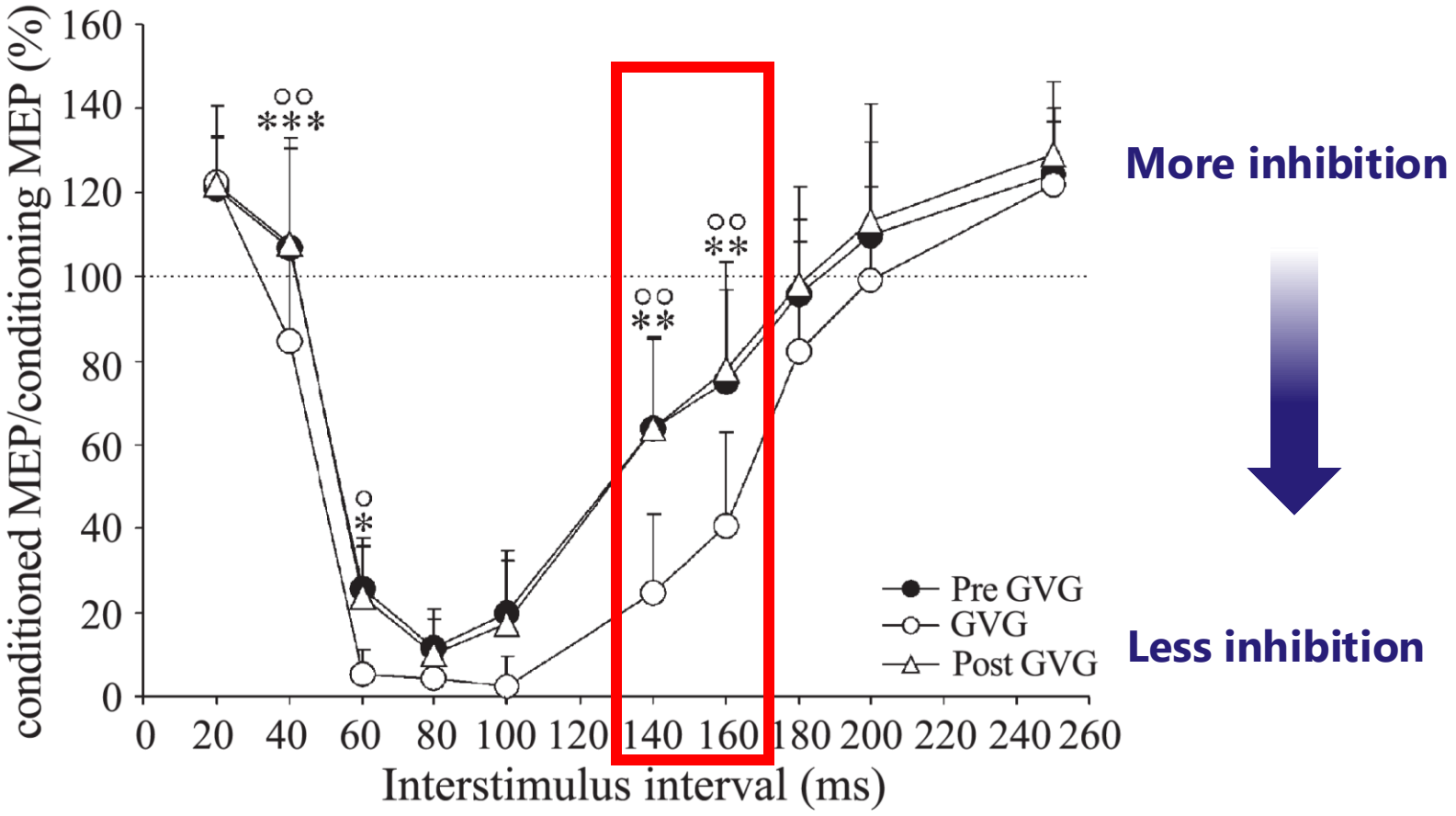
©2025 Ovid Therapeutics | All Rights Reserved

LICI provides the ability to compare with healthy volunteers treated with 1st generation GABA-AT inhibitor, vigabatrin

- VGB showed greatest impact & statistical significance on the Long interval intracortical inhibition (LICI) between 140 ms – 160 ms.
- Marking a sign of slowed cortical response to paired pulse stimuli (GABAergic inhibition)
- Significance and response diminished ~200 ms

VIGABATRIN PERFORMANCE AT TX DOSE ON THE LONG INTERVAL INTRACORTICAL INHIBITION (150 ms)

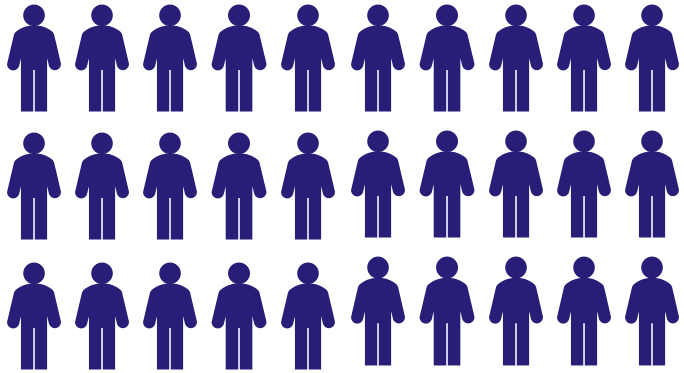
Figure 1B



Pierantozzi M, Marciani MG, Palmieri MG, Brusa L, Galati S, Caramia MD, Bernardi G, Stanzione P. Effect of Vigabatrin on motor responses to transcranial magnetic stimulation: an effective tool to investigate in vivo GABAergic cortical inhibition in humans. Brain Res. 2004 Nov 26;1028(1):1-8. doi: 10.1016/j.brainres.2004.06.009. PMID: 15518635

©2025 Ovid Therapeutics | All Rights Reserved

Strong, differentiated safety profile in treated participants



30 treated participants

No treatment-related AEs or SAEs

- Most common AE was headache

No vision or ocular findings associated with treatment

- All participants followed for 30 days post-treatment; including taking retinal imagery

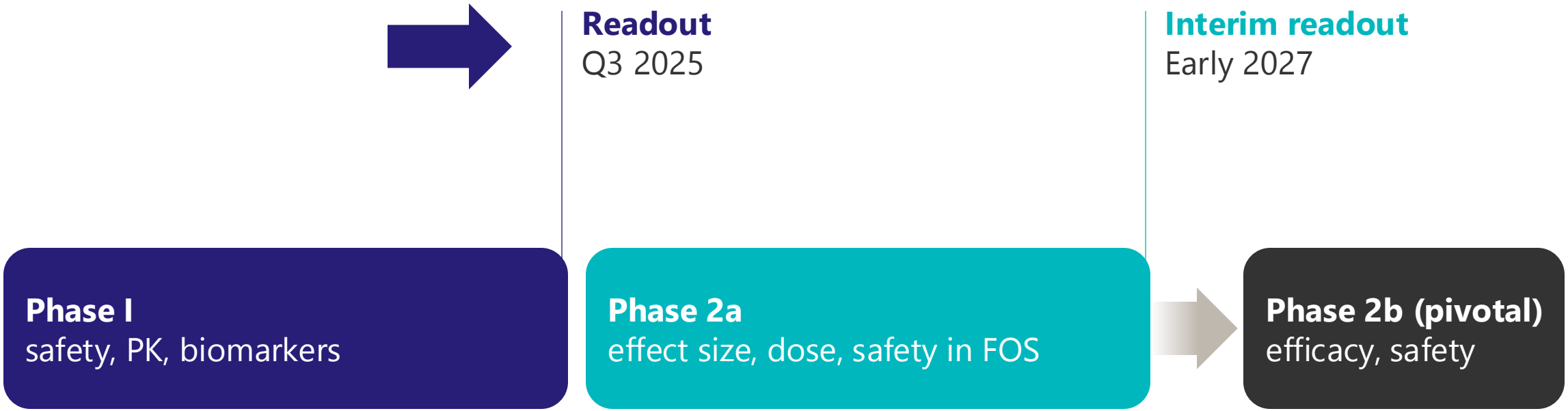
Comprehensive ocular safety metrics

- Best corrected visual acuity
- Indirect dilated ophthalmoscopy
- Automated threshold visual field perimetry
- Fundus photography
- Optical coherence tomography (OCT)

OVID data on file as of March 9, 2025

©2025 Ovid Therapeutics | All Rights Reserved

Phase 2 design:
Leads to two potential de-risking events in next 24 mos.



©2025 Ovid Therapeutics | All Rights Reserved

Clinical strategy intended to de-risk program; validate doses for Phase 2

What trial intends to deliver	When & how

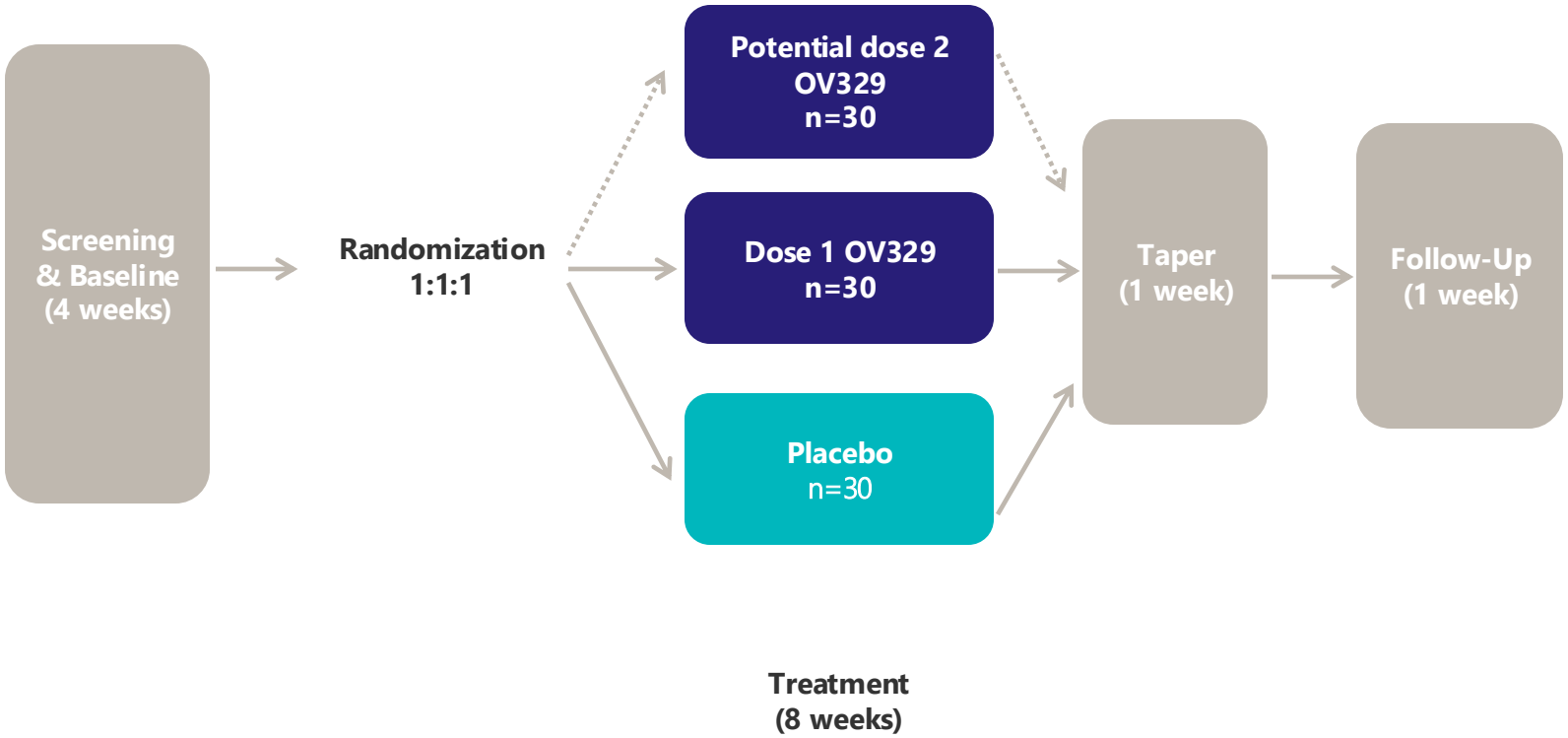
Drug hits the biological target
Increases markers of cortical inhibition
Dampens excited neurons
No safety issues
	Phase 1 topline (Q3 2025)
	• Pre- and post-treatment response
	• Target engagement - Increased GABA in brain
	• Pharmaco-dynamic effect:
	  • Inhibitory activity on EEG or transcranial magnetic stimulation
	  • Comparability with therapeutic dose of first-generation medicine
	• Ophthalmic and retinal safety

Competitive anti-convulsant profile **Dose confirmation for pivotal trials** **Differentiated safety from 1st generation**	**Phase 2a interim readout in adults with focal seizures (Q1 2027)** • Seizure reduction effect size • Competitive seizure reduction profile • Dose response • Safety

©2025 Ovid Therapeutics | All Rights Reserved

Phase 2a trial design in patients with focal-onset seizures

Evaluating the safety, tolerability, and antiseizure effect of OV329

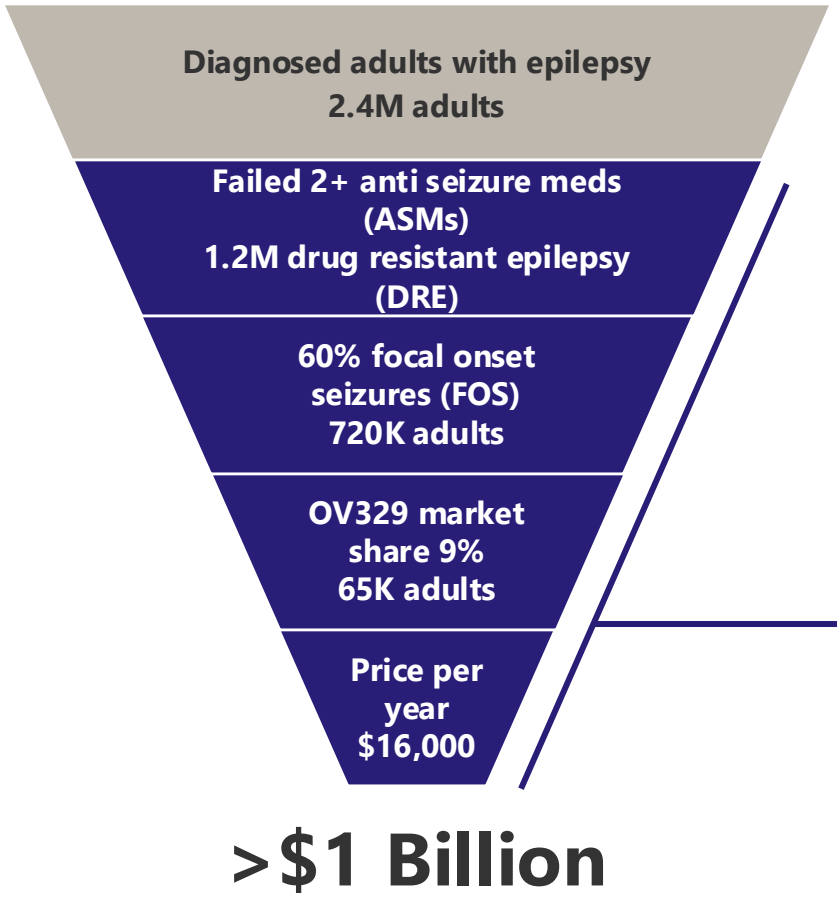


- Seizure reduction effect size
- Building comprehensive safety package
- Phase 2b dose & design guidance
- Preliminary readout in early 2027

©2025 Ovid Therapeutics | All Rights Reserved

Unique, well-tolerated MoAs are rewarded in epilepsy, even in a competitive DRE market

Substantial opportunity within the DRE segment



>$1 Billion

Key: Voltage-gated Ion Channel Target | GABAergic | Synaptic Target | Other / Mixed / Unknown

Focal / Partial seizures

1L	Carbamazepine	Levetiracetam	Oxcarbazepine
	Phenytoin	Eslicarbazepine	Lacosamide
2L	Clobazam	Lamotrigine	Topiramate
	Rufinamide	Zonisamide	
Refractory + polypharmacy (~40%)	OV329 *In Phase 1*	XEN1101	XCOPRI
		Fycompa perampanel	BRIVIACT (brivaracetam)

Reimbursement & coverage dynamics remain favorable. Polypharmacy well covered

J Med Chem. 2012 Jan 26; 55(2): 567–575; 2. J Am Chem Soc. 2018 Feb 14; 140(6): 2151–2164

©2025 Ovid Therapeutics | All Rights Reserved

Broader lifecycle opportunity for a safe GABA-AT inhibitor is significant

Initial intended indication

Focal seizures in adults with drug resistant epilepsy

Potential follow-on indications

Focal seizures in developmental epileptic encephalopathies

Post-surgical & peri-operative pain

Substance abuse and alcohol withdrawal

©2025 Ovid Therapeutics | All Rights Reserved

Portfolio of direct activators of potassium chloride cotransporter 2 (KCC2)

Potentially transformational target that is a fulcrum rebalance inhibitory/excitatory signaling in many diseases of the brain

Potential first-in-class direct activators

OV350 (IV) Phase 1 topline readout estimated for Q4 2025

OV4071 (oral) Phase 1 initiation expected in Q2 2026

IP through 2046 (assumes five-year patent term extension)

9 method-of-use patents filed

© Copyright 2025 Ovid Therapeutics

KCC2 maintains inhibitory/excitatory balance & normalizes neuronal activity[1]

"Master switch" for a broad spectrum of neurological disorders

where hyperexcitability accelerates disease progression

Precise MoA exclusively expressed in the brain

To rebalance network hyperexcitability & mitigate safety effects associated with other potassium chloride transporters that are broadly expressed

Final "common pathway"

Downstream of many genetic and acquired causes of neurological dysfunction and central to maintain GABAergic inhibitory tone

Impossible to "over modulate"

Energetically challenging to over-extrude chloride from the neuron which should contribute to a cleaner profile

1. Pressey et al. "Chloride transporters controlling neuronal excitability."

©2025 Ovid Therapeutics | All Rights Reserved

KCC2 regulates GABA inhibition by maintaining neuronal chloride homeostasis

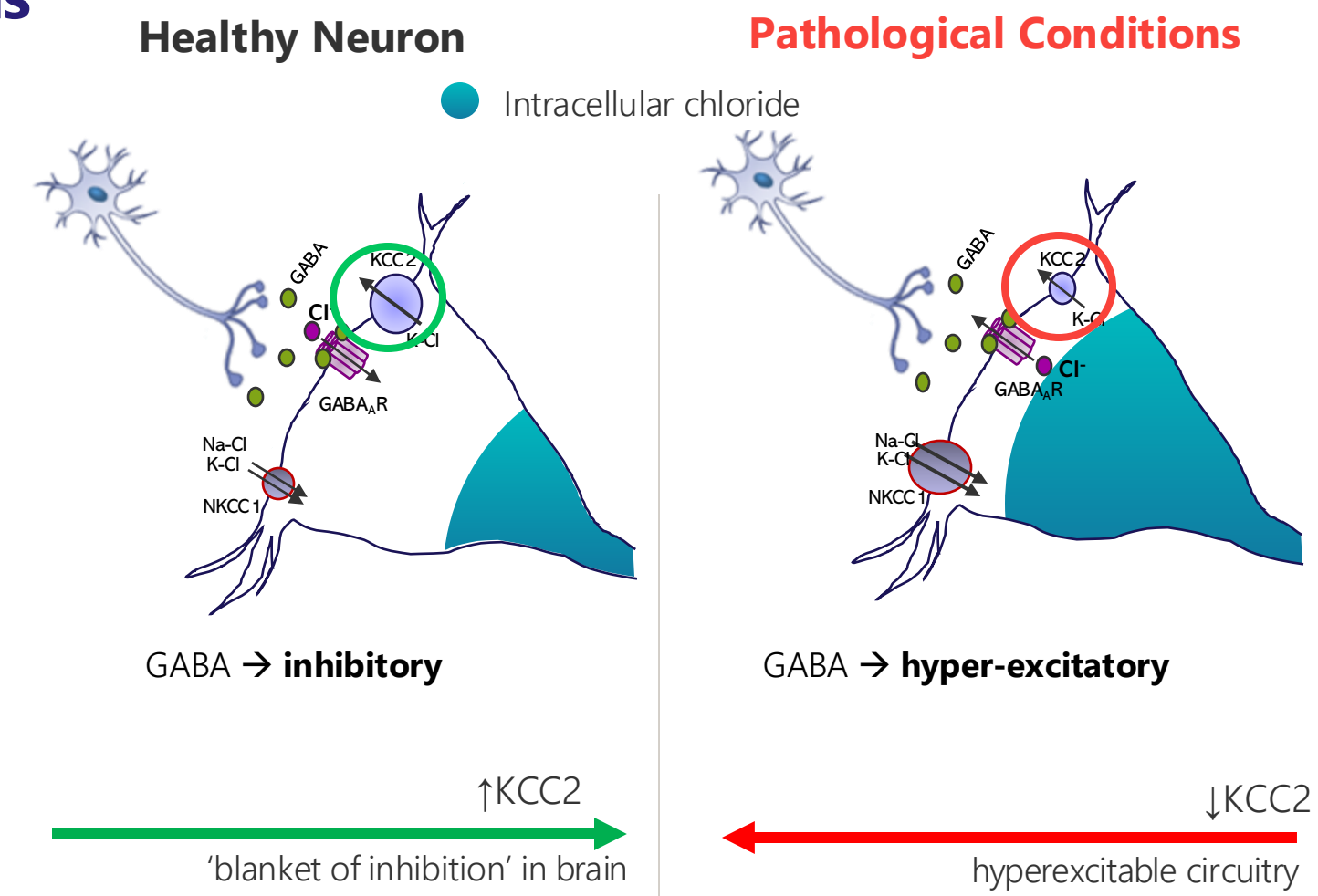
KCC2 regulates chloride gradient

- Chloride gradient is necessary for GABA-ergic inhibition at the synapse

Manages the passive inward flux of chloride through activated ion channels

Maintaining low intracellular chloride is required for:

- The efficacy of hyperpolarization
- Shunting inhibition mediated by GABAergic signaling in neurons



Activating KCC2 restores the brain's natural braking system, fixing network defects that cause excessive neural activity (hyperexcitability)

Pressey et al. "Chloride transporters controlling neuronal excitability", https://doi.org/10.1152/physrev.00025.2021

Illustrations adapted from publication by Phan Q. Duy, Miao He, Zhigang He & Kristopher T. Kahle (2020) Preclinical insights into therapeutic targeting of KCC2 for disorders of neuronal hyperexcitability, Expert Opinion on Therapeutic Targets, 24:7, 629-637, DOI: 10.1080/14728222.2020.1762174

©2025 Ovid Therapeutics | All Rights Reserved

Why direct activation of KCC2 matters

- Binds directly to KCC2 transporter—modulating function independently of upstream pathways
- Effective regardless of phosphorylation, BDNF signaling, or disease-driven dysregulation
- Enables dose-controlled, predictable, and rapid onset of action
- Avoids tachyphylaxis and downstream adaptation seen in indirect pathways
- Limits unintended modulation of off-target signaling cascades
- Reduces risk of hyperpolarization beyond physiological range

© Copyright 2025 Ovid Therapeutics

Franchise of KCC2 direct activators in development

OV350 & OV4071 behave similarly in phenotypic screens

	OV350	OV4071	OV4041
Formulation	Intravenous	Oral Intramuscular injection / SubQ	Oral Intramuscular injection
Indication	**First-in-human potential proof-of-mechanism**	**Psychosis in Parkinson's disease & Lewy body dementias**	**Generalized anxiety disorder Rett syndrome**
Characteristics (from disease & phenotypical models)	• Antipsychotic & anticonvulsant activity • No AEs • No sedation • Rapid acting	• Antipsychotic • 20x potency over OV350 • 60x EC50 reached in repeat dosing • Excellent tolerability • Consistent plasma exposure • No sedation	• Anxiolytic • Antipsychotic • Anticonvulsant activity
Anticipated milestones	Phase 1 in progress Safety, tolerability/PK completion Q4 2025	• Currently in IND-enabling • Phase 1 initiation Q2 2026 Topline results Q1 2027	• Initiating IND-enabling studies late 2025/early 2026 • IND submission late 2026

©2025 Ovid Therapeutics | All Rights Reserved

In Phase 1: OV350

Dose dependent exposure

- Strong activity in psychosis phenotypic & disease models
- Dose-exposure-PD relationship demonstrated in animals
- Behaves like atypical antipsychotics
- Outperforms to clozapine in phencyclidine-induced psychosis model

Safety & margins

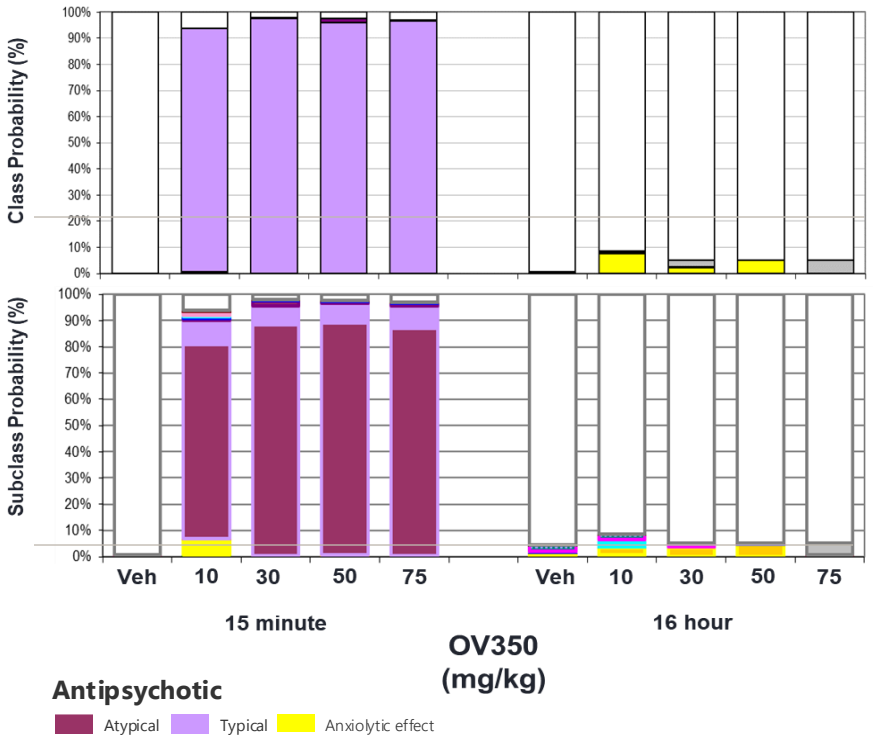
- Started Phase 1 dosing Q1 2025
- Permissive safety package
- No observed adverse effect level (NOAEL) in rats & dogs
- No evidence of sedation
- Ames & in vitro mutagenesis tests negative (i.e., clean)
- DDI assessment completed with no concerns

©2025 Ovid Therapeutics | All Rights Reserved

OV350 elicits potent, robust, rapid and reversible antipsychotic activities

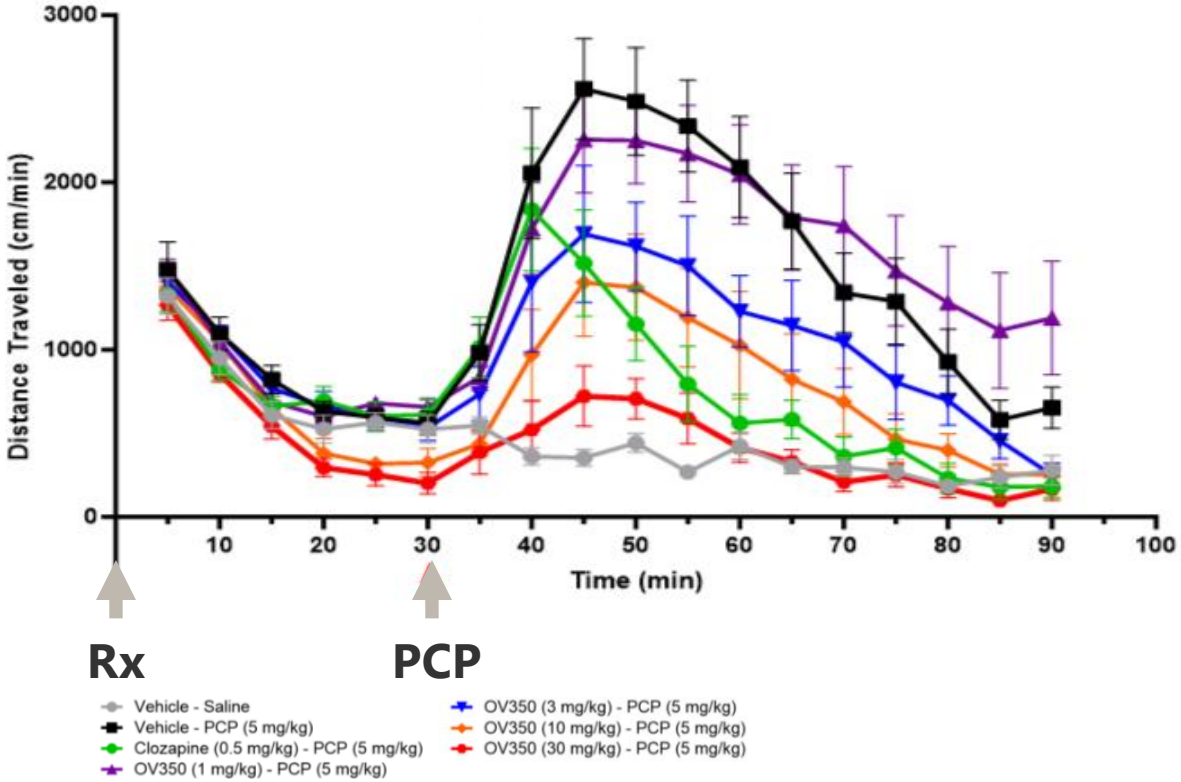
Profile similar to atypical antipsychotic in SmartCube® screen

- Onset of effect within 15 minutes
- Dose response starting at 10 mg/kg; disappears in 16 hours
- No sedation or other adverse behavior effects observed up to 75 mg/kg
- Minor anxiolytic effects observed (yellow)



Phencyclidine-induced psychosis (PCP) model

- OV350 dose-dependently inhibited PCP induced hyperlocomotion
- Model is characterized by: Confusion, excitation, aggression, paranoia, hallucinations, and can be experimentally measured by hyperlocomotion
- No evidence of sedation



Ovid data on file

©2025 Ovid Therapeutics | All Rights Reserved

OV350 enables potential first-in-class characterization & rapid path to patients for oral KCC2 direct activators

- Phase 1 to demonstrate acceptable safety (for a first-in-class mechanism)
- Enables ability to potentially establish PK/PD relationship & apply insights to oral programs
- Characterize safety, tolerability, PK for non-CNS indications

Plan to initiate OV4071 (oral) program in Q2 2026, which behaves similarly to OV350 in phenotypic models

- Seek to establish proof-of-mechanism in patients via Phase 1b
- Program currently in IND-enabling

©2025 Ovid Therapeutics | All Rights Reserved

IND-enabling studies: OV4071, an oral direct activator

Potent, dose dependent PK/PD

- >20x potency than OV350
- Strong activity in psychosis phenotypic & disease models
- Dose dependent response in animals

Safety & margins

- 60x in vivo EC50 reached in repeat dosing
- Excellent tolerability in repeat dosing
- Consistent plasma exposure
- Progressing in non-GLP toxicology studies

Large opportunity

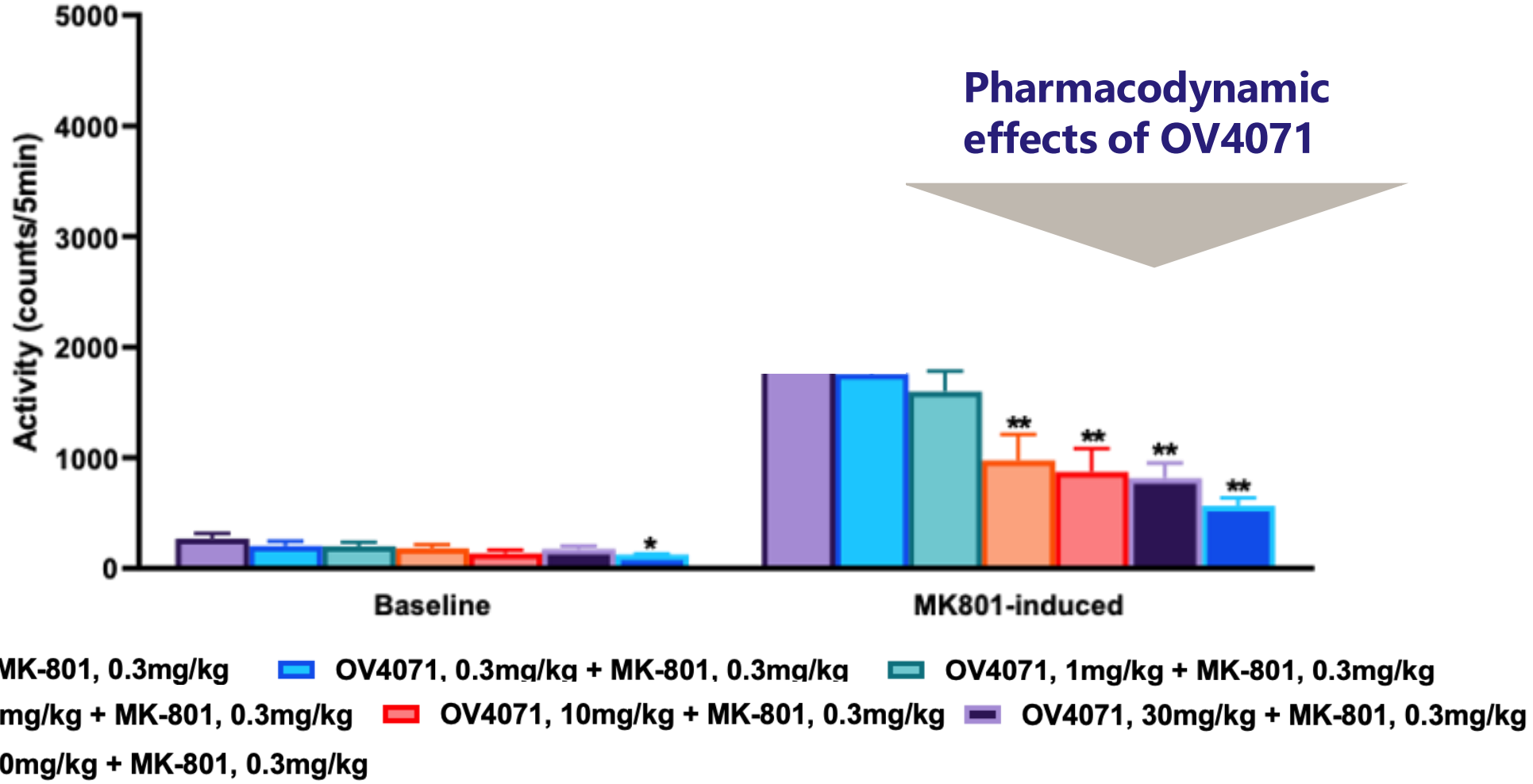
- Psychosis with Parkinson's disease, Lewy body dementia
- Potential to expand to Alzheimer's agitation

Ovid data on file

©2025 Ovid Therapeutics | All Rights Reserved

OV4071 dose dependent response in schizophrenia psychosis model

Uses an NMDAR antagonist (MK801) to elicit dopamine release in the basal ganglia



Ovid data on file

©2025 Ovid Therapeutics | All Rights Reserved

Psychosis is optimal indication for KCC2 direct activation

Synaptic dysfunction is fundamental to the pathophysiology of psychosis

- Initiated by biological event in PD and LBD psychosis (pathological alpha synuclein)
- Exacerbated and perpetuated by continuous neurotransmitter imbalance

Excitatory/inhibitory imbalance is an important contributor to synaptic dysfunction

- While there are many drivers of excitation GABA is the key inhibitory neurotransmitter

Alterations in GABAergic transmission in different parts of the brain drive different clinical manifestations

- Reduced GABA and altered signaling documented in prefrontal cortex (PFC) in patients with psychosis
- A direct link between PFC E-I imbalance and cognitive deficits identify KCC2 reduction as a common molecular alteration across models of psychosis
- GABA concentrations by MRS in the visual cortex of PD patients with visual hallucinations
- Reduced GABAergic activity in the visual cortex of DLB patients

Taken together with data in pharmacodynamic models, strong support for psychosis as 1st indication for OV4071

Murkerjee et al.(pre-print)
Shine, 2014
Firbank et al., 2018
Khundakar et al., 2016
Bowman et al., 2017

©2025 Ovid Therapeutics | All Rights Reserved

OV4071 indication represents a significant unmet need

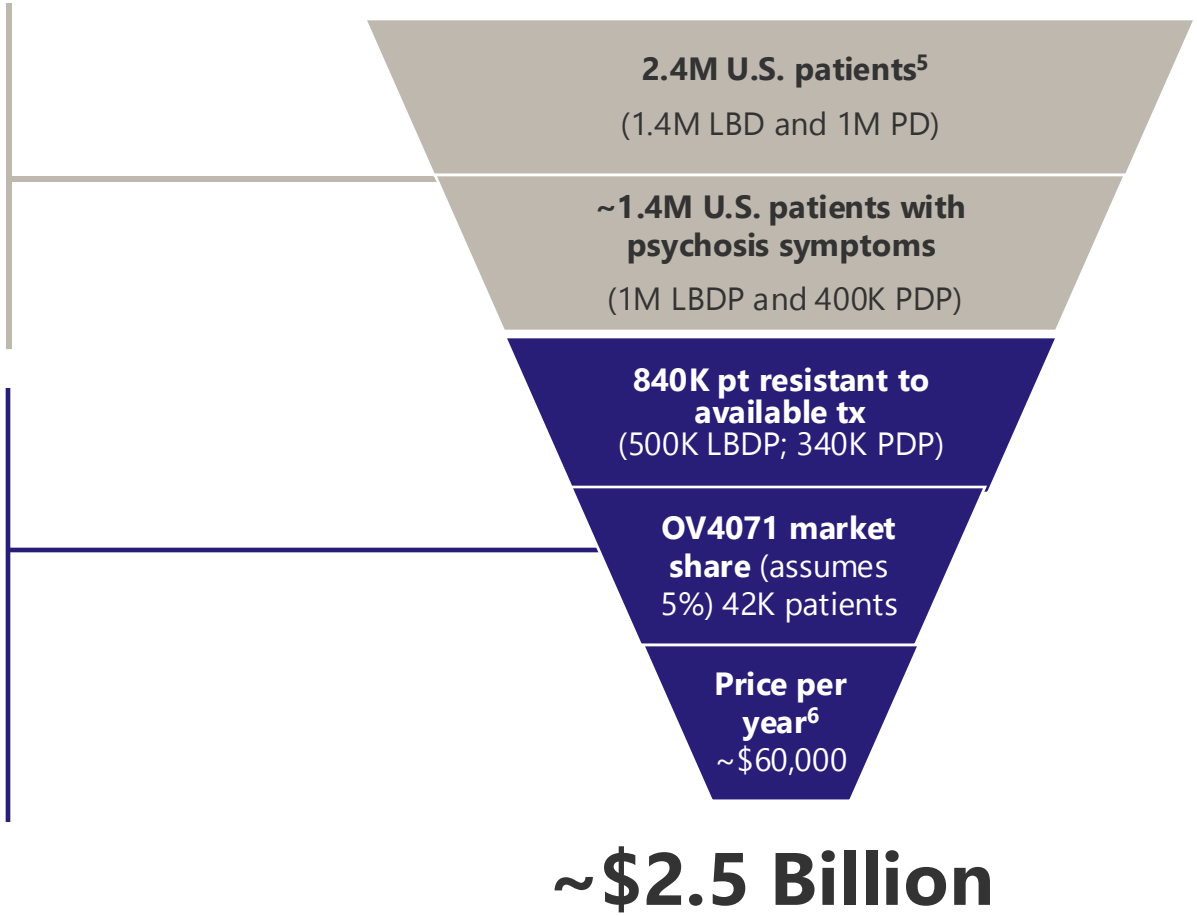
Target population	• Psychoses associated with neuronal synuclein disorders (NSD): Parkinson's disease psychosis • Lewy body dementia psychosis (both NSDs)[1]
MoA relevance	Regulation of chloride balance is lost and GABA inhibitory signaling does not occur normally, KCC2 is downregulated in certain forms of psychosis[2]
Enrichment strategy	Neuronal synuclein disorder positive (can be confirmed via skin biopsy test & CSF) Screening for hyposmia
Unmet need	• Only 12% of patients respond to SoC (Nuplazid)[3] • Atypical antipsychotics contraindicated • High morbidity, mortality and cost • Highest risk of nursing home placement[4]
Value proposition	Most patients do not have a therapy that works >70% of PDP and LBD patients will experience psychosis symptoms[5,6]

1. Simuni et al. Lancet Neurol. 2024 Feb;23(2):178-190. doi: 10.1016/S1474-4422(23)00405
2. Hyde et al. J Neuroscci. 2011 Jul 27;31(30):11088–11095
3. Nuplazid USPI: https://www.nuplazid.com/pdf/nuplazid-prescribing-information.pdf
4. Goetz and Stebbins. Neurology. 1993 Nov;43(11):2227-9. doi: 10.1212/wnl.43.11.2227
5. Diederich et al, Nat Rev Neurol 5, 331–342 (2009). https://doi.org/10.1038/nrneurol.2009.62.
6. Lewy Body Dementia Association: https://www.lbda.org/emergency-room-treatment-of-psychosis/

©2025 Ovid Therapeutics | All Rights Reserved

A large opportunity for OV4071: Parkinson's disease psychosis and Lewy body dementia psychosis

- LBD and PD prevalence growing as baby boomers age and life span increases
- Nearly all LBD patients (75%)[1] and up to half of PD (20-40%)[2] experience psychosis symptoms, requiring treatment
- In >50% of cases approved treatments have limited efficacy or have severe side effects/ contraindicated[3]
- Use of Nuplazid® (the SoC) is limited due to limited efficacy and a Boxed Warning[4]
- No approved treatment options for LBDP



~$2.5 Billion

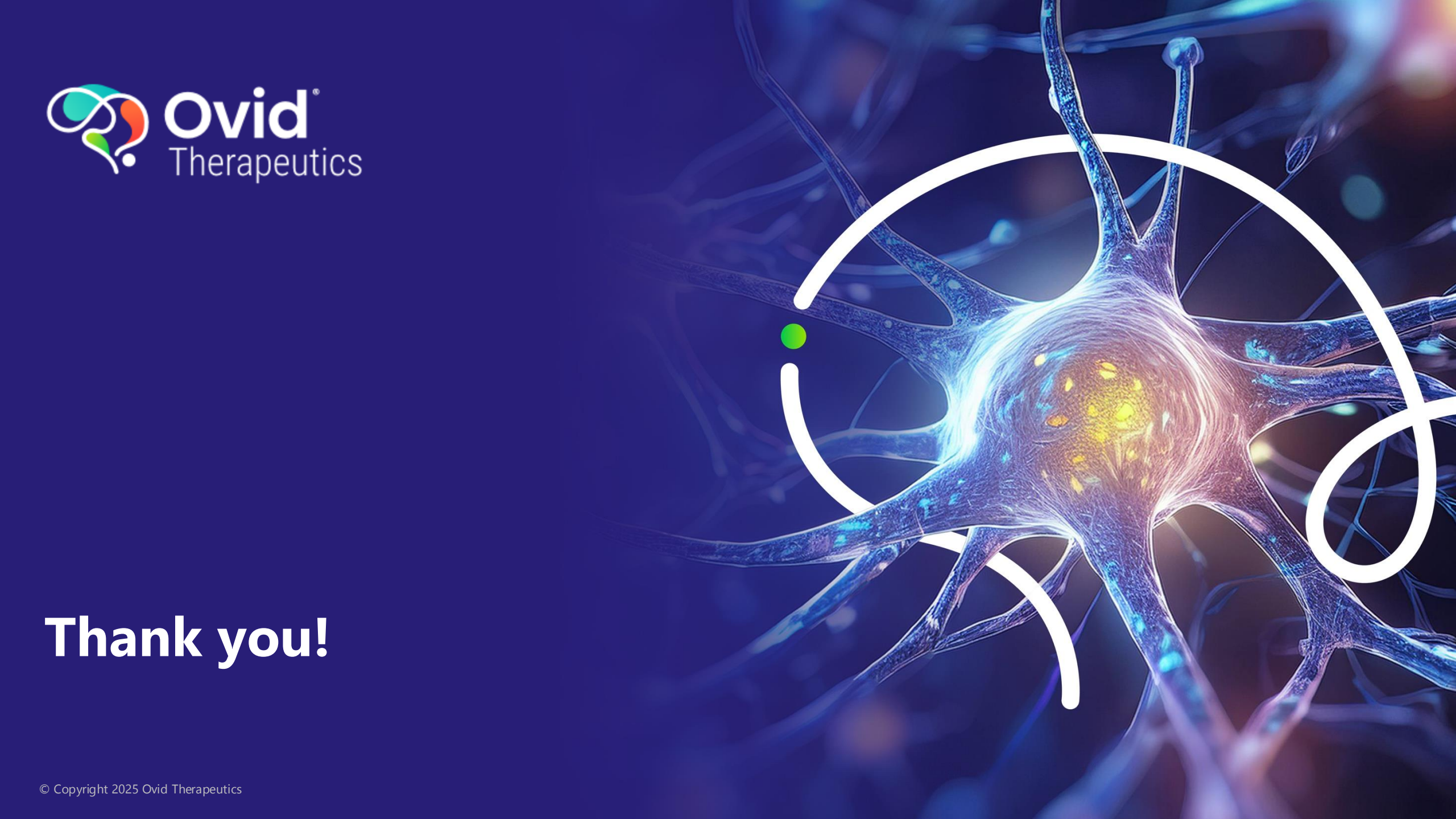
1. Diederich et al, Nat Rev Neurol 5, 331–342 (2009). https://doi.org/10.1038/nmeurol.2009.62.
2. Parkingson Foundation: https://www.parkinson.org/understanding-parkinsons/non-movement-symptoms/hallucinations-delusions
3. Lewy Body Dementia Association: https://www.lbda.org/emergency-room-treatment-of-psychosis/ and https://www.lbda.org/treatment-options/ Nuplazid efficacy: https://www.nuplazidhcp.com/efficacy-data#67uOuSEzX31CdL3A5qcY1b
4. Nuplazid USPI: https://www.nuplazid.com/pdf/nuplazid-prescribing-information.pdf
5. LBD: https://www.lbda.org/about-lbd/ and PD: https://www.parkinson.org/understanding-parkinsons/statistics#:~:text=Nearly%20one%20million%20people%20in,90%2C000
6. https://www.nuplazidhcp.com/pdf/nuplazid-distribution-fact-sheet.pdf

Multiple near-term pipeline milestones

Milestone	Timing
OV329: Topline data (biomarkers for clinical effect and target engagement, safety & tolerability)	Q3 2025
OV350: 1st in-human KCC2 direct activator safety and tolerability data	Q4 2025
OV329: Phase 2a trial initiation	Q1 2026
OV4071: First oral KCC2 direct activator entering humans	Q2 2026
OV329: Phase 2a topline data	Q1 2027

© Copyright 2025 Ovid Therapeutics

Ovid Therapeutics



Thank you!

© Copyright 2025 Ovid Therapeutics