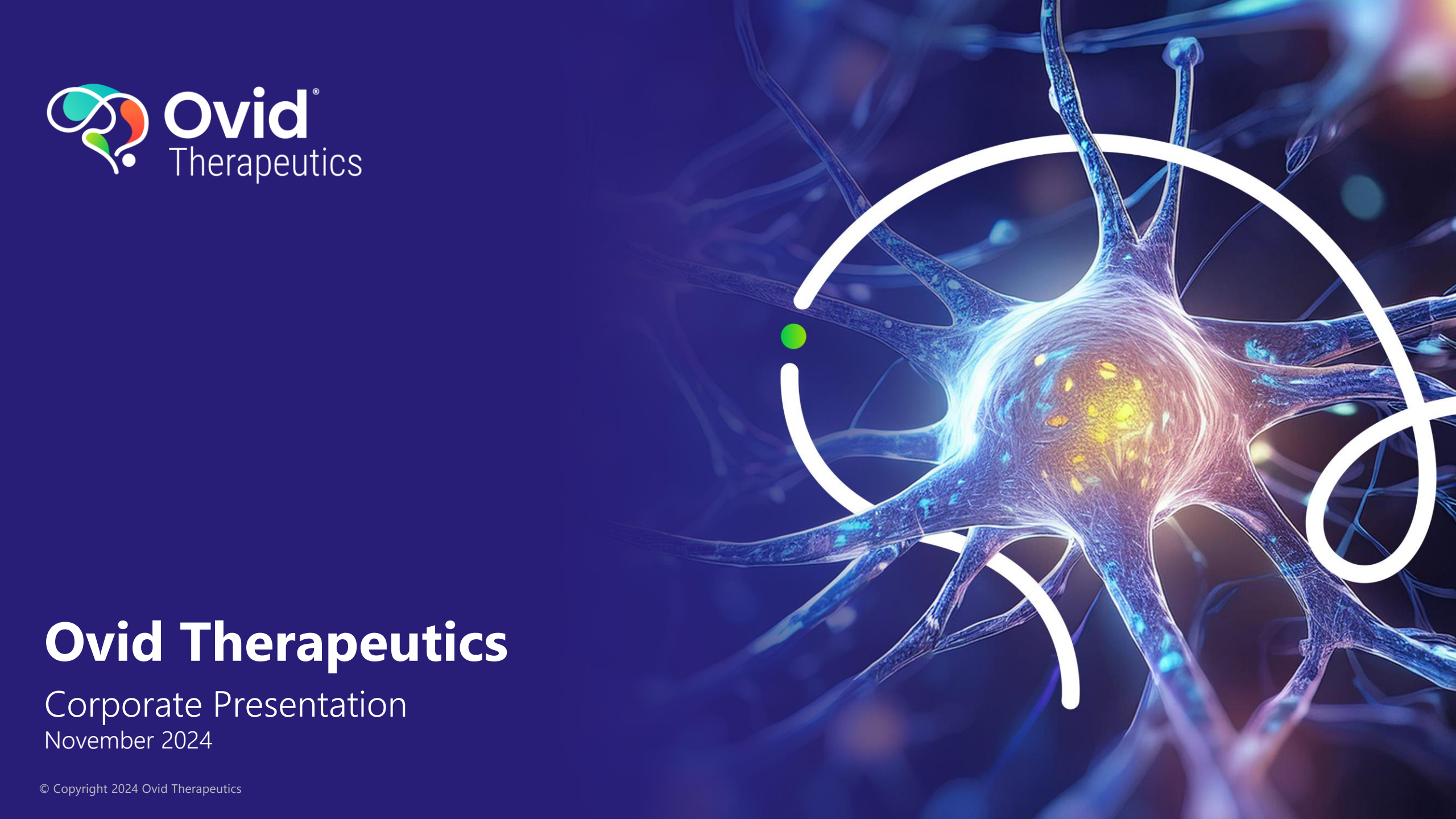


Ovid Therapeutics

Corporate Presentation

November 2024

Forward looking statement

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 its cash runway, and the expectation that it will support the advancement of Ovid's pipeline; statements regarding the expected timing of the initiation, completion, and results and data of Ovid's clinical studies; the potential to add additional cohorts to the Phase 1 MAD study of OV329, expected timing of completion of the study and expected timing of data presentation; the expected timing of submission of a regulatory application for a Phase 1 trial of OV350 IV and, the expected timing of initiation of the trial and expected timing of data presentation; Ovid's evaluation of the results of recently completed competitor trials to OV888/GV101 for CCM; the potential use and development of OV329, OV350 and other compounds from Ovid's library of direct activators of KCC2, and OV888/GV101 and other ROCK2 inhibitors; the potential therapeutic opportunity of OV329, OV350 and other compounds from Ovid's library of direct activators of KCC2, and OV888/GV101 and other ROCK2 inhibitors; the potential use of OV329 to treat neuronal hyperexcitability; 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 indication opportunities; the clinical and regulatory development of KCC2 compounds in the Company's library including OV350, OV4071, OV4000 series and OV5000 series; the suitability of the Company's library of novel, direct KCC2 transporter activators for a range of formulations and administrations; the potential development and therapeutic opportunity of OV888/GV101; and the potential safety, selectivity and potency of OV888/GV101 and other ROCK2 inhibitors; 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 factors 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, risks related to Ovid's ability to achieve its financial objectives, the risk that Ovid may not be able to realize the intended benefits of its technology or its business strategy, risks related to 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 and risks to Ovid's or any of its partners' abilities to meet anticipated deadlines and milestones. 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 November 12, 2024, and in future filings Ovid makes with the SEC. Any forward-looking statements contained in this press release 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.

OUR FOCUS

Foundational biological targets

Implicated in neuronal hyperexcitability, neuroinflammation or neurovascular dysfunction

Substantial therapeutic opportunities

across neurological and neuropsychiatric conditions with deep unmet need

Highly specific small molecules

Harnessing a scientific revolution in mechanistically targeted small molecules for the central nervous system

Cash balance of $62.7 million

expected to support pipeline to H2 2026[1]

1. As of September 30, 2024

OUR SCIENCE

Unique mechanisms with broad therapeutic potential

Proven developers
of candidates to mitigate neuronal hyperexcitability

OV329, a next generation GABA-aminotransferase inhibitor

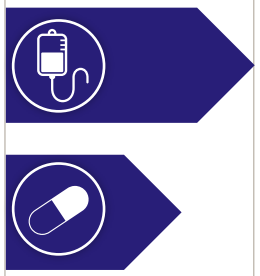
Pioneers of KCC2
direct activation

OV350, OV4071 & portfolio of direct activators

Translators of ROCK2 inhibition in the brain

OV888/GV101, a highly selective ROCK2 inhibitor

Differentiated pipeline, advancing in the clinic

Programs	Indication	Preclinical	Phase 1	Phase 2	Phase 3	Anticipated Milestones
OV329 GABA-aminotransferase inhibitor	• Conditions with neuronal hyperexcitability					Phase 1 estimated readout in 2025 Topline timing to be updated following discussions with regulators
OV350 & KCC2 LIBRARY KCC2 direct activator	• Neuropsychiatric • Neurodevelopmental • Neurodegenerative • Seizures • Pain					Phase 1 initiation expected in Q1 2025
OV888/GV101[1] Selective ROCK2 inhibitor Collaboration with: GRAVITON BIOSCIENCE CORPORATION	• Cerebral cavernous malformations • Undisclosed neurovascular indications					Pausing initiation of Phase 2 program in CCM to evaluate insights from recently completed competitor programs OV888/GV101 intravenous formulation in preclinical development

1. Graviton is conducting development of OV888/GV101 capsule through Phase 2, which will be directed by a Joint Development Committee that includes members from both Graviton and Ovid.

Third quarter corporate updates

Presented OV329 head-to-head preclinical ocular results

- Demonstrated no ocular accumulation in tissue as compared to confirmatory accumulation with vigabatrin
- Further data to be presented at American Epilepsy Society Conference in December 2024

Pipeline actions

- **OV888/GV101**: Together with Graviton Biosciences, paused initiation of OV888/GV101 Phase 2 trial in CCM to evaluate insights from recently completed competitor trials
- **OV329:** Seeking to add further cohorts to OV329 Phase 1 trial based upon supportive human safety data
- **OV350**: Anticipating to file for a Phase 1 safety trial for OV350, a first-in-class direct activator of KCC2 in Q4 2024
- **KCC2 Library:** Advancing multiple preclinical KCC2 direct activator and ROCK2 inhibitor compounds and formulations

Extended cash runway to H2 2026[1]

1. As of September 30, 2024

Anticipated pipeline milestones

Program	Key milestones	Anticipated Timing
OV329	Results of Phase 1 SAD/ MAD with MRS and TMS biomarkers	2025 Detailed timeline for topline and Phase 2 to be provided following discussions with regulators
OV350 IV	Regulatory submission for first-in-human study of KCC2 direct activator	Q4 2024
	Phase 1 study initiation	Q1 2025
	Results from Phase 1 study	Early 2026
OV888/ GV101	Cleared by regulators to proceed with Phase 2, but pausing to assess insights from competitor trials in CCM to inform potential approach in future	Paused

OV329

A next-generation GABA-aminotransferase inhibitor for the potential treatment of conditions of neuronal hyperexcitability

A potential best-in-class, next-generation GABA-aminotransferase inhibitor

Validated target: Inhibition of GABA-aminotransferase (GABA-AT)

- Similar mechanism of action to approved anti-seizure medicine, Sabril (vigabatrin), a 1st generation GABA-AT inhibitor
- Increases endogenous levels of GABA, the inhibitory neurotransmitter
- >100 times greater potency over vigabatrin in nonclinical studies[1]

Therapeutic index: OV329 seeks to avert the ocular toxicity of vigabatrin

- Vigabatrin has no therapeutic index; it was found some patients experience retinal degradation & irreversible blindness[1]
- OV329 has established a therapeutic index within which no ocular toxicity or sedation has been observed

Unique pharmacokinetic/pharmacodynamic profile: Low doses with prolonged effect

- OV329 has durable effect on GABA-AT inhibition due to irreversible enzyme inhibition
- Repeat dosing leads to profound tonic GABA current changes

Potential portfolio in a product: Multiple indications in which neuronal hyperexcitability is implicated

1. Yang J, et al. Vigabatrin-induced retinal toxicity is partially mediated by signaling in rod and cone photoreceptors. PLoS One. 2012;7(8):e43889. doi: 10.1371/journal.pone.0043889. Epub 2012 Aug 30.

A next-generation GABA-AT targeting improved safety & tolerability

OV329 seeks to improve upon vigabatrin, a 1st-generation GABA-AT inhibitor

Sabril profile:

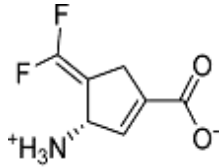
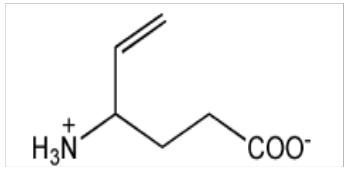
- Effective seizure reduction, but no therapeutic window[1]
- Approved for treatment of:[2]
  - Forms of infantile spasms
  - Complex partial seizures associated with tuberous sclerosis complex
- Post-approval, vigabatrin associated with progressive visual field loss from retinal toxicity[3]
- Black Box Warning
- REMS required
- Safety concerns deter use & prescribing

Sabril Peak Sales in U.S. with Ocular Safety Label

(Not representative of global sales)[4]

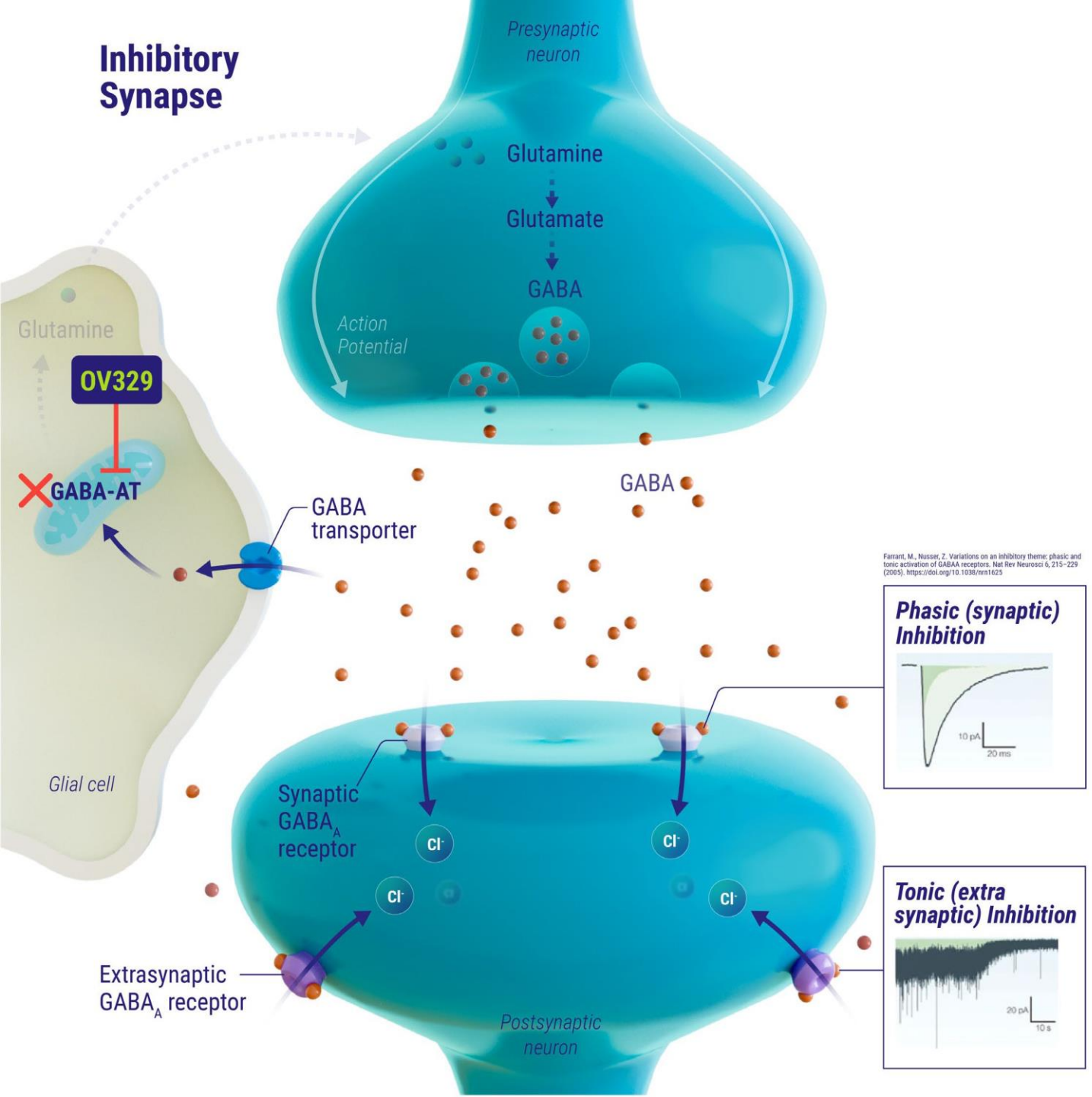
1. Maguire et al., 2010; Epilepsia, 51(12):2423–2431, 2010
2. Pesaturo KA, Spooner LM, Belliveau P. Vigabatrin for infantile spasms. Pharmacotherapy. 2011 Mar;31(3):298-311. doi: 10.1592/phco.31.3.298. PMID: 21361740.
3. BMJ 1997;314:180–181
4. Evaluate Pharma

Factors contributing to OV329 safety profile differentiation

	OV329	Vigabatrin
Molecule		
Potency	IC_{50}: ~0.1 - 0.3 μM	IC_{50}: ~60 – 100 μM
Exposure characteristics	Reduced exposure ($T_{1/2}$ ~1.0 Hour) coupled with prolonged PD duration	$T_{1/2}$ >5.0 Hours Both R (inactive) & S (active) enantiomers
Mechanism of enzyme inhibition	Electrostatic (irreversible) (more sophisticated chemistry, primarily enamine pathway) [2]	Covalent modification of GABA-AT (reversible) (early generation chemistry, primarily Michael addition pathway) [1]
Purity	Only active, (S) enatiomer	Mixture of active (S) and inactive (R) enantiomers
Inhibition	Phasic + tonic (synaptic & extrasynaptic)	Phasic (synaptic)
Therapeutic index (as measured in Sprague Dawley rats, a proxy model used to assess ocular safety)	✓	✗ None – toxicity seen at therapeutic dose

»» Improved potency (>100x), PK/PD and established therapeutic index[2]

1. J Med Chem. 2012 Jan 26; 55(2): 567–575; 2. J Am Chem Soc. 2018 Feb 14; 140(6): 2151–2164
2. Feja et al. OV329, a novel highly potent γ-aminobutyric acid aminotransferase inactivator, induces pronounced anticonvulsant effects in the pentylenetetrazole seizure threshold test and in amygdala-kindled rats. Epilepsia. 2021 Dec;62(12):3091-3104. doi: 10.1111/epi.17090. Epub 2021 Oct 7.



OV329 mechanism of action

GABA is the major inhibitory neurotransmitter in brain

OV329 substantially reduces GABA-AT activity, a key enzyme responsible for degrading GABA, thus elevating GABA levels[1]

OV329 increases phasic and tonic inhibitory neurotransmission at GABAergic synapses[2]

Creating an inhibitory milieu in the synapse and extrasynaptic region

Curbs excessive neuronal excitation and reduces seizures

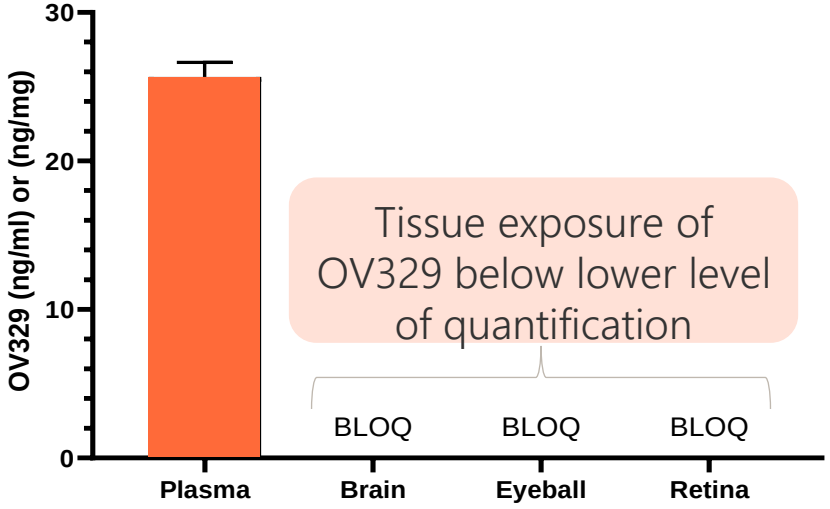
1. Silverman RB. Chem Rev. 2018 Apr 11;118(7):4037-4070. doi: 10.1021/acs.chemrev.8b00009. Epub 2018 Mar 23. PMID: 29569907; PMCID: PMC8459698.
2. Feja, Malte et al. "OV329, a novel highly potent γ-aminobutyric acid aminotransferase inactivator, induces pronounced anticonvulsant effects in the pentylenetetrazole seizure threshold test and in amygdala-kindled rats." Epilepsia vol. 62,12 (2021): 3091-3104. doi:10.1111/epi.17090

Head-to-head: Ocular safety preclinical study versus vigabatrin

Lack of retinal accumulation of OV329 supports differentiated ocular safety profile vs vigabatrin[1,2]

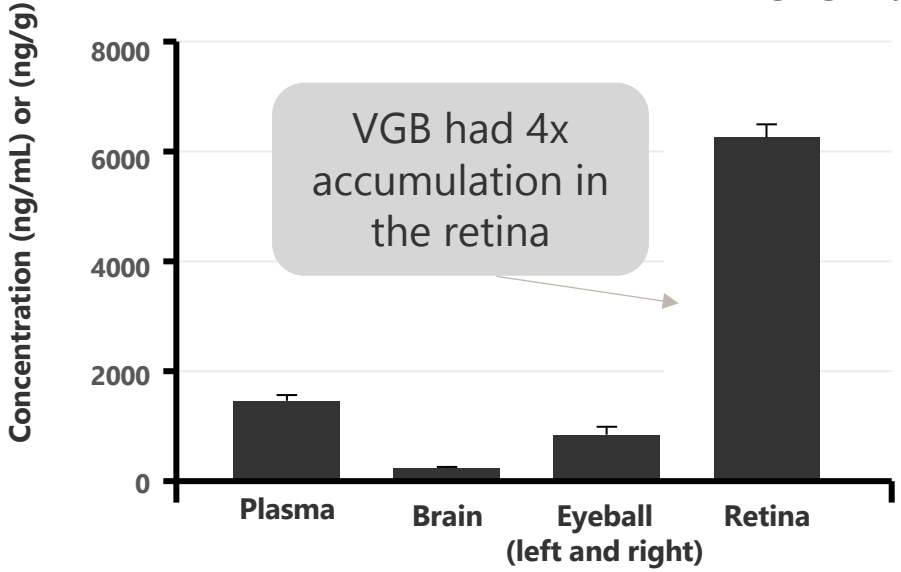
OV329

Mean Plasma and Tissue Concentration 5.0 mg/kg/day



VIGABATRIN

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



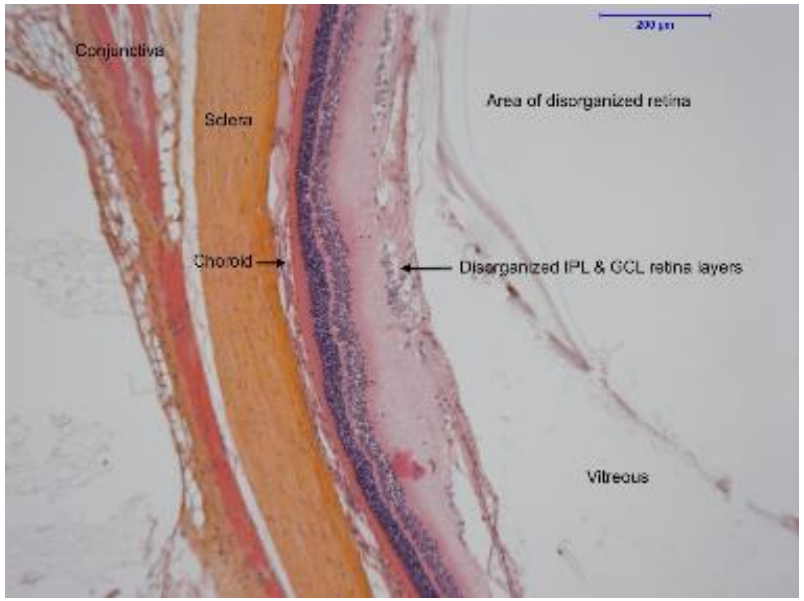
FINDINGS[1,2]

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

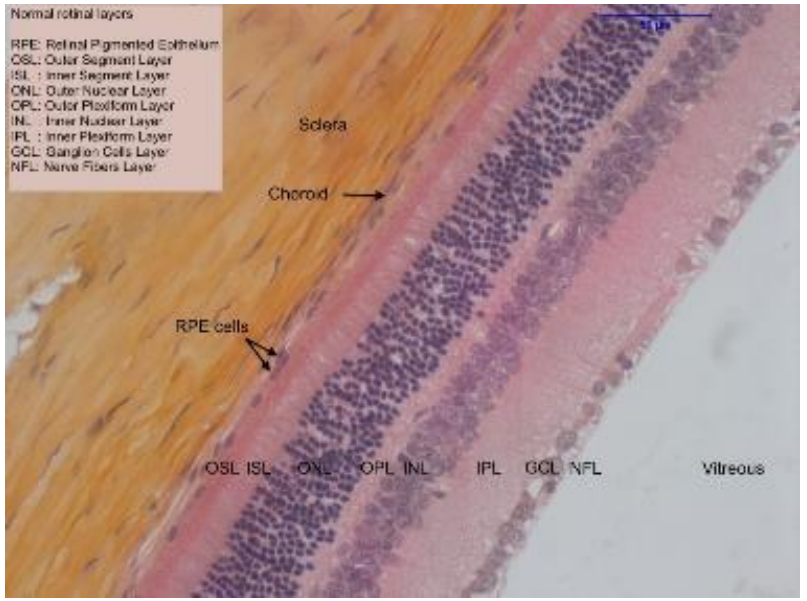
1. Tsai, J., et al. (2024). *Evaluation of the Potential Accumulation of OV329 in the Brain, Retina, and Eye Following Continuous Infusion.* Poster presented at the 2024 Epilepsy Pipeline Conference.
2. Detailed results from the head-to-head animal study will be presented at the 2024 American Epilepsy Society conference

No ocular effects seen following chronic exposure with OV329 (3 mg/kg)

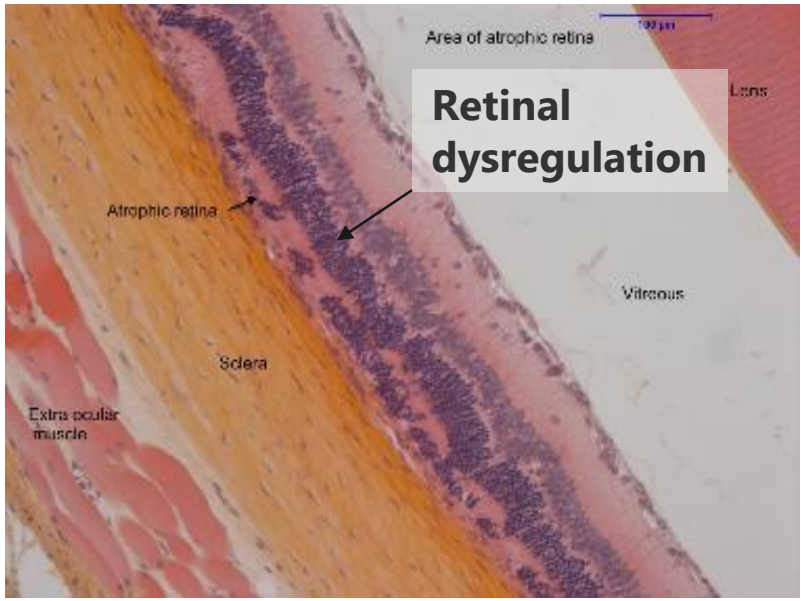
Vehicle



OV329 3.0 mg/kg



Vigabatrin 300 mg/kg



No ocular effects seen in 3 mg/kg OV329, q.d. and vehicle groups in rats at Day 45[1]

Ocular effects seen in more than half of rats treated with Vigabatrin (300 mg/kg)[1]

1. 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.

Collective preclinical findings suggest a differentiated safety profile

OV329:

- Is >100x more potent than vigabatrin in nonclinical stuides[1]
- Penetrates the brain, as it is found in animal plasma, which is reinforced by findings by many animal seizure models comparable to vigabatrin[2]
- Demonstrates rapid tissue clearance properties and half life (1.5 hours) compared to vigabatrin (4 hours)[2]
- In ocular accumulation studies, OV329 cleared tissue and was undetectable in the retina, eye or brain tissue whereas vigabatrin was found to accumulate in 48 hours[2]
- Demonstrates prolonged pharmacodynamic effect through both phasic and tonic (synaptic & extra-synaptic) inhibition[3]

1. Feja et al. OV329, a novel highly potent γ-aminobutyric acid aminotransferase inactivator, induces pronounced anticonvulsant effects in the pentylenetetrazole seizure threshold test and in amygdala-kindled rats. Epilepsia. 2021 Dec;62(12):3091-3104. doi: 10.1111/epi.17090. Epub 2021 Oct 7.
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.
3. 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.

Anti-convulsant activity reaffirmed by 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	+	+	+	+	+	+	+	+	+

OV329 has the potential to be a franchise in a product

Chronic
Applications
(Oral Formulations)

- Treatment resistant epilepsies
- Developmental epileptic encephalopathies with focal seizures
- Seizures associated with Tuberous sclerosis complex
- Neonatal spasms
- Focal seizures

Acute
Applications
(IV formulations-IND ready[1])

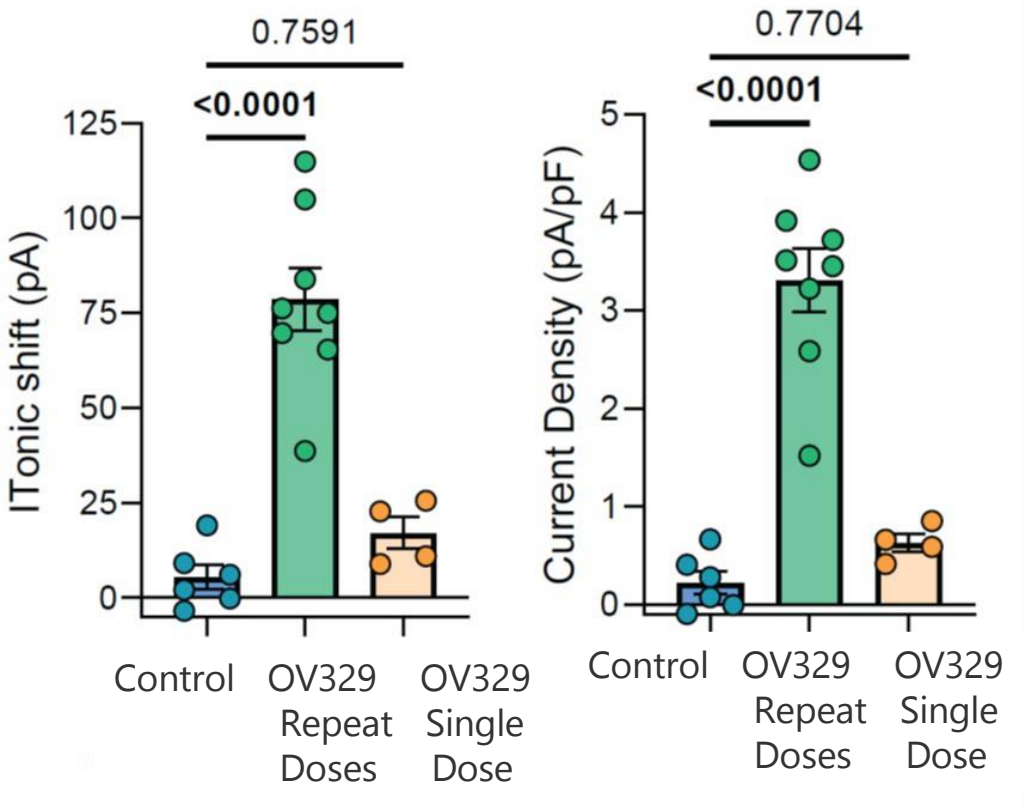
- Post-surgical pain
- Refractory status epilepticus
- Seizures from alcohol withdrawal

Multiple potential indication opportunities driven by endogenously increasing GABA levels

1. OV329 IV has filing package ready, however program was deprioritized in August 2024 to prioritize corporate resources

Repeat low dosing induced GABA tonic current creating inhibitory milieu[1]

Change in tonic current (mice)



OV329 achieves modulation of GABAergic inhibition by both phasic (synaptic) and tonic current (extra-synaptic)

Chronic dosing of OV329 leads to sustained GABA increase and enhanced tonic current (extra-synaptic)

The tonic GABA inhibitory response is likely to modulate neuronal hyperexcitability more effectively

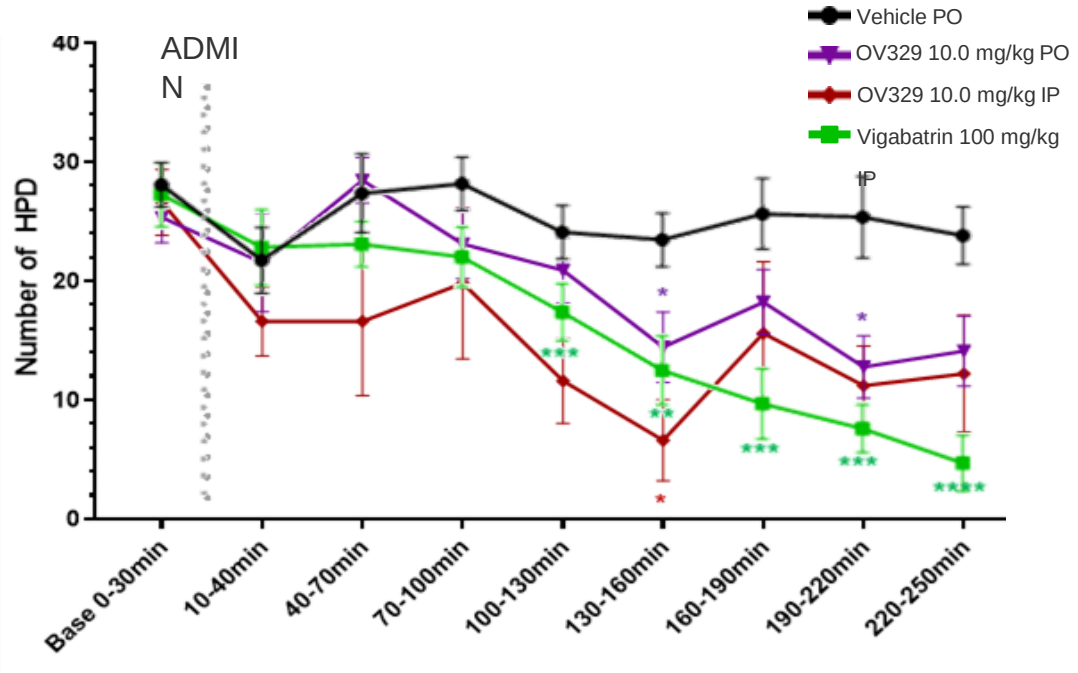
Suggests repeated, low dosing of OV329 in humans should suppress seizures

OV329 in repeat, low doses delivers tonic and phasic inhibition enabling prolonged seizure reduction

1. 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.

OV329 significantly reduces seizures in the MTLE mouse model in single & repeat dosing

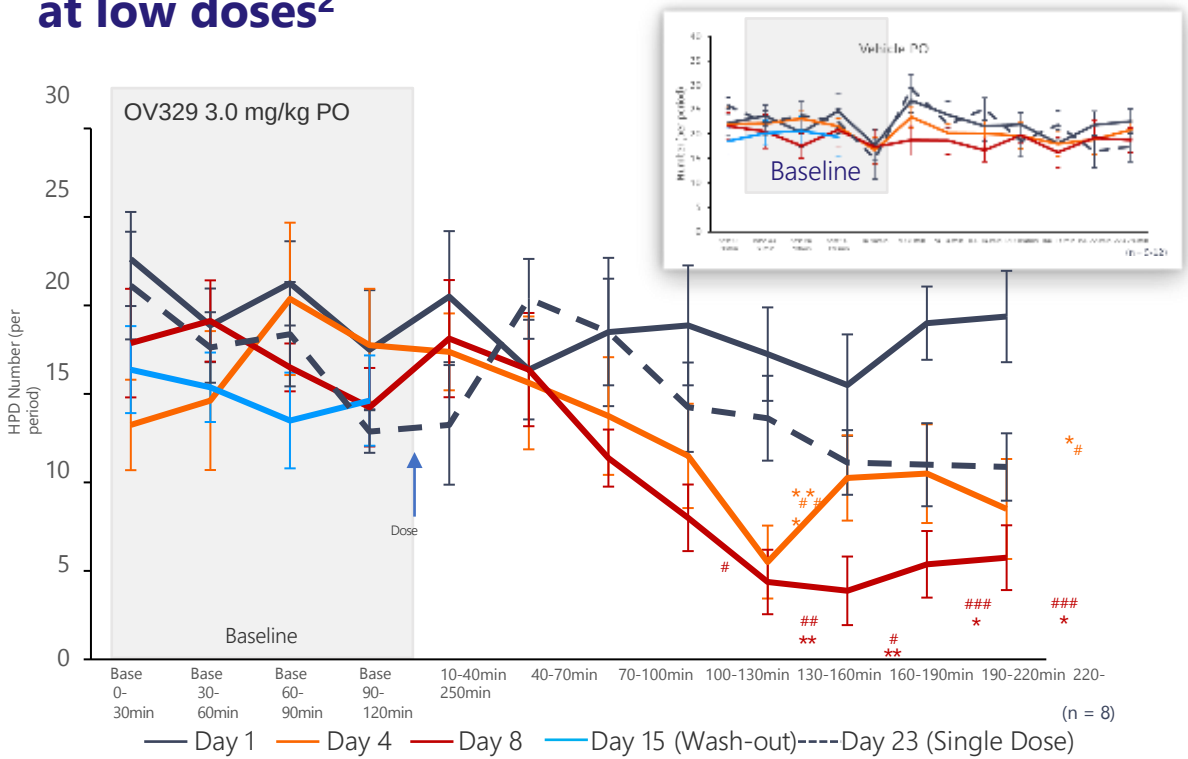
Single administration of OV329 reduced the number of hippocampal paroxysmal discharges (HPDs)[1]



- OV329 achieved a 55% reduction in seizure activity after IP administration
- OV329 achieved a 46% reduction after oral administration

Data are expressed as mean ± SEM. *,**, ***, ****: p < 0.05, 0.01, 0.001 or 0.0001, respectively

Repeat dosing of OV329 demonstrates activity in the MTLE mouse model of drug-resistant epilepsy at low doses[2]



- 3.0 mg/kg in mice reduced seizures (HPD) by ~70% compared to baseline levels at Day 8

Data are expressed as mean ± SEM. *,**: p < 0.05, 0.01 vs Baseline; #, ##:p < 0.05, 0.01 vs Day 1

1. Duveau, et al. *CNS Neurosci Ther.* 2016;22(6):497-506; [2]Sarmiere, PD et al. *American Epilepsy Society Meeting*, 2021.
2. Mukherjee, J., et al. (2022). *OV329, a Next-Generation GABA-AT Inhibitor, Suppresses Hippocampal Paroxysmal Discharges Following Repeat Dosing in a Mouse Model of Mesial Temporal Lobe Epilepsy.* Poster presented at the American Epilepsy Society 2022.

OV329 clinical development program

Phase 1 safety, tolerability and biomarker study

3 SAD cohorts completed in healthy volunteers

2 MAD cohorts completed dosing; no serious adverse events reported

Measures safety, tolerability & other ophthalmic monitoring, such as:

- Best corrected visual acuity
- Fundus photography
- Indirect dilated ophthalmoscopy
- Automated threshold visual field perimetry
- Optical Coherence Tomography

Two biomarkers for effect and target engagement pending:

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

Next steps:

Pending final results; engaging regulators to add cohorts to increase dosing opportunities in future Phase 2 programs

KCC2 library & OV350

Potential first-in-class direct activators of the KCC2 co-transporter

Ovid's KCC2 direct activators portfolio a franchise of potential neurotherapeutics

Unique target

Direct activator of KCC2

Key to regulating neuronal excitation

Exclusively expressed in CNS

Multiple compounds & formulations

100+ unique compounds

Different pharmacologic properties

Multiple formulations:

- Intravenous
- Oral pill
- Intramuscular injection

Differentiated potential target product profile

No sedation observed

Low risk of over modulation

Initial IP to 2041

BROAD THERAPEUTIC OPPORTUNITY

KCC2 is a fundamental biological target in maintaining inhibitory/excitatory balance[1]

Precision mechanism of action to rebalance network hyperexcitability

Targets synaptic inhibition, the “final common pathway” downstream of many genetic and acquired causes of epilepsy, and other neurological conditions

Converges on a broad spectrum of neurodegenerative disorders where hyperexcitability accelerates disease progression

Central to maintaining GABA-ergic inhibitory tone

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

KCC2 is the main regulator of GABA inhibition by maintaining neuronal chloride homeostasis[1]

Regulates chloride gradient

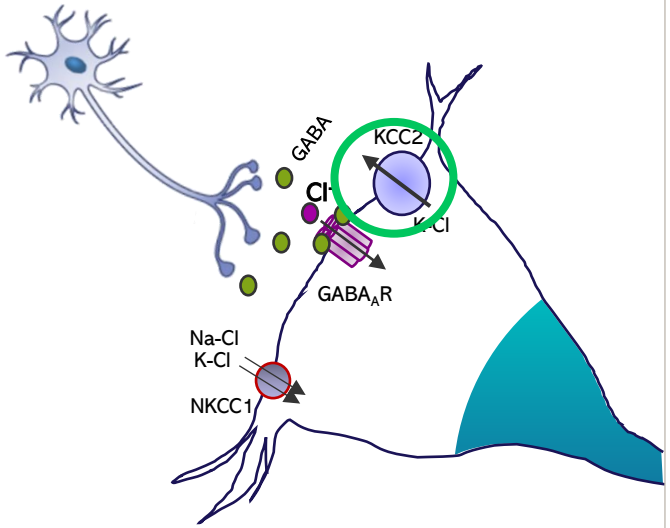
Manages the passive inward flux of Cl^- through activated ion channels

Maintaining low intracellular chloride is critical for:

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

KCC2 activation: Restores inhibition 'A battery to recharge interneurons'

Healthy Neuron



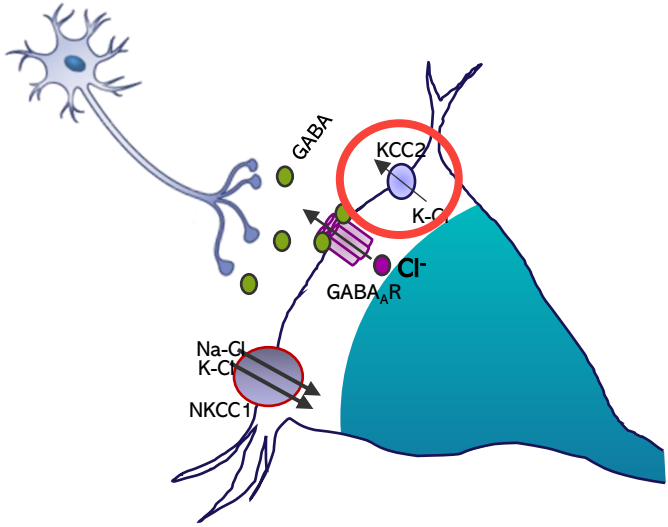
GABA → **inhibitory**

Intracellular chloride

Healthy ↑KCC2

'blanket of inhibition' in brain

Pathological Conditions



GABA → **hyper-excitatory**

Intracellular chloride

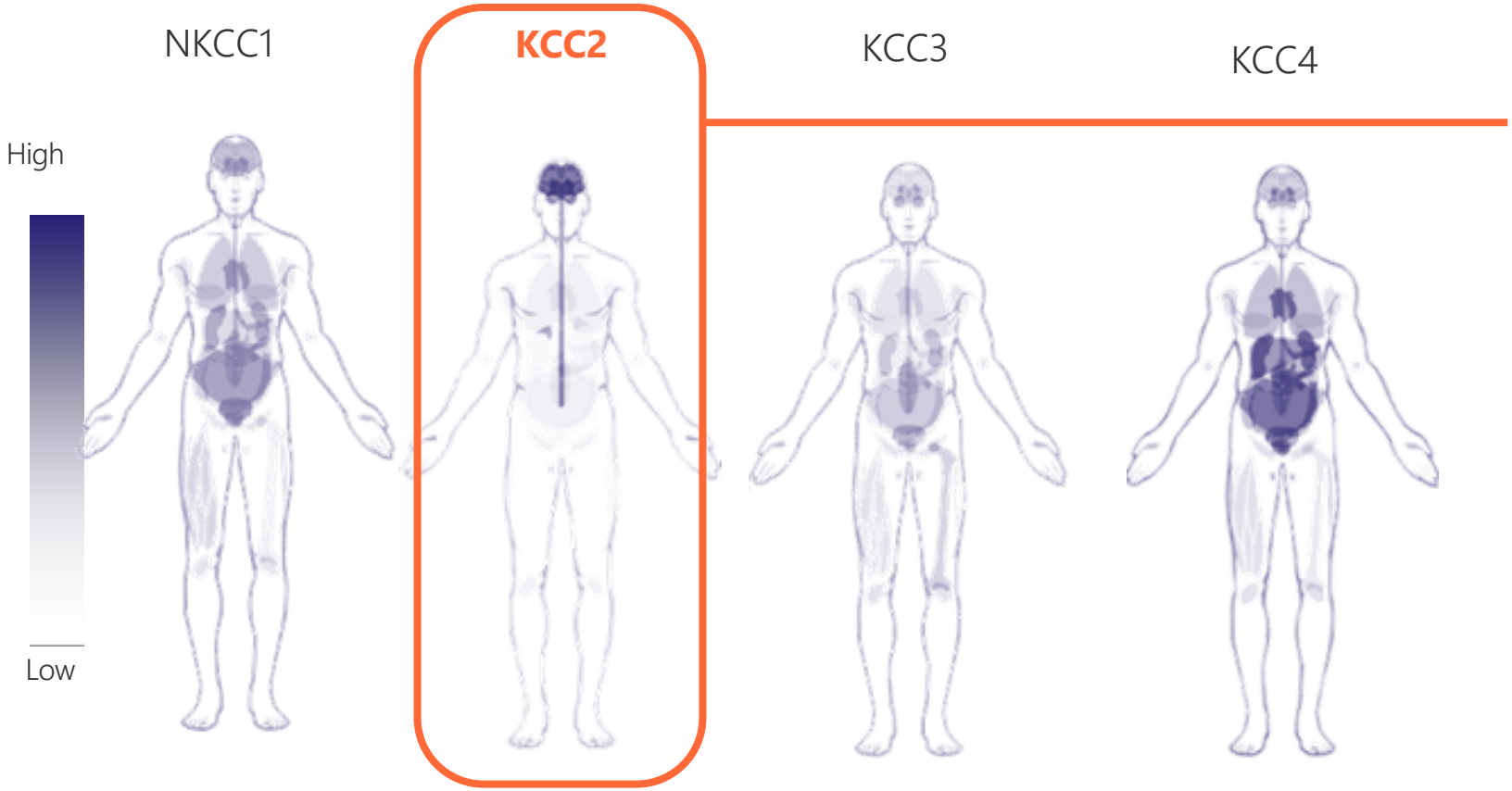
Pathology↓KCC2

hyperexcitable circuitry

1. Cheung, D.L., Toda, T., Narushima, M. et al. KCC2 downregulation after sciatic nerve injury enhances motor function recovery. Sci Rep 13, 7871 (2023). 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

KCC2 is exclusively expressed in the CNS

KCC2 expression vs. other transporters modulating chloride homeostasis



Isoform of the potassium chloride cotransporter family

KCC2 expression only in neurons

Not systemic expressed in other organs

Ovid's portfolio of KCC2 direct activators

Direct activators with unique chemistry

High degree of specificity with lower risk of off-target effects

4 compounds in active development with unique characteristics

Multiple formulation opportunities

No sedation observed using in vivo models

Phase 1, first-in-human for OV350, anticipated by Q1 2025

Potent, specific & brain-penetrant small molecules with electrophysiologic activity[1]

POTENCY

- HT screen of 1.3 million compounds using an established thallium TI influx assay in HEK-293 cells overexpressing KCC2
- Threshold of >30% potentiation of KCC2 activity at EC50 of <30 mM
- All KCC2 leads have single digit uM potency for KCC2

SPECIFICITY

- Hits filtered in assays overexpressing KCC3, KCC4, or NKCC1
- All kinase inhibitors are eliminated on PKC isoforms
- Direct binding of KCC2 was demonstrated by cellular thermal shift assay (CETSA)

ELECTRO-PHYSIOLOGIC ACTIVITY

- Patch clamp recordings measuring reversal potentials in hippocampal neurons showed significantly reduced EGABA at EC50 dose, demonstrating significant decrease in intracellular Cl- levels

1. Jarvis et al Direct activation of KCC2 arrests benzodiazepine refractory status epilepticus and limits the subsequent neuronal injury in mice. Cell Rep Med. 2023 Mar 21;4(3):100957. doi: 10.1016/j.xcrm.2023.100957. Epub 2023 Mar 7. PMID: 36889319; PMCID: PMC10040380.

KCC2 direct activator portfolio has substantial therapeutic opportunity

OVID KCC2 Direct Activator Potential Indications

Chronic (PO & IM Formulations)	**Sub-acute** (PO & IM Formulations)	**Acute** (IV & IM Formulations)
• Seizures • Psychosis • Schizophrenia • Bipolar syndrome • Huntington's disease • Neurodevelopmental disorders • Pain	• Seizures • Psychosis • Schizophrenia • Bipolar syndrome • Pain	• Acute psychosis • Traumatic brain injury • Spinal cord injury • Pain

Broad continuum of opportunities driven by unifying disease biology and enabling chemistry

Lead program from portfolio: OV350, a first-in-class KCC2 direct activator

Specificity

Directly binds to KCC2 (surface plasmon resonance and thermal shift assay)

No off-target effects on kinases regulating KCC2 activity (PKC, SPAK, WNK)

Penetrance

Small molecule (MW<500)

Excellent brain penetration

Potential for biomarker

OV350

Disease model activity

Comparable activity to clozapine

Prominent anti-psychotic activity

Anti-convulsant activity

Neuroprotective signals

Safety

No evidence of sedation in animals

Permissive safety package

OV350 elicits rapid antipsychotic-like effects in preclinical screen

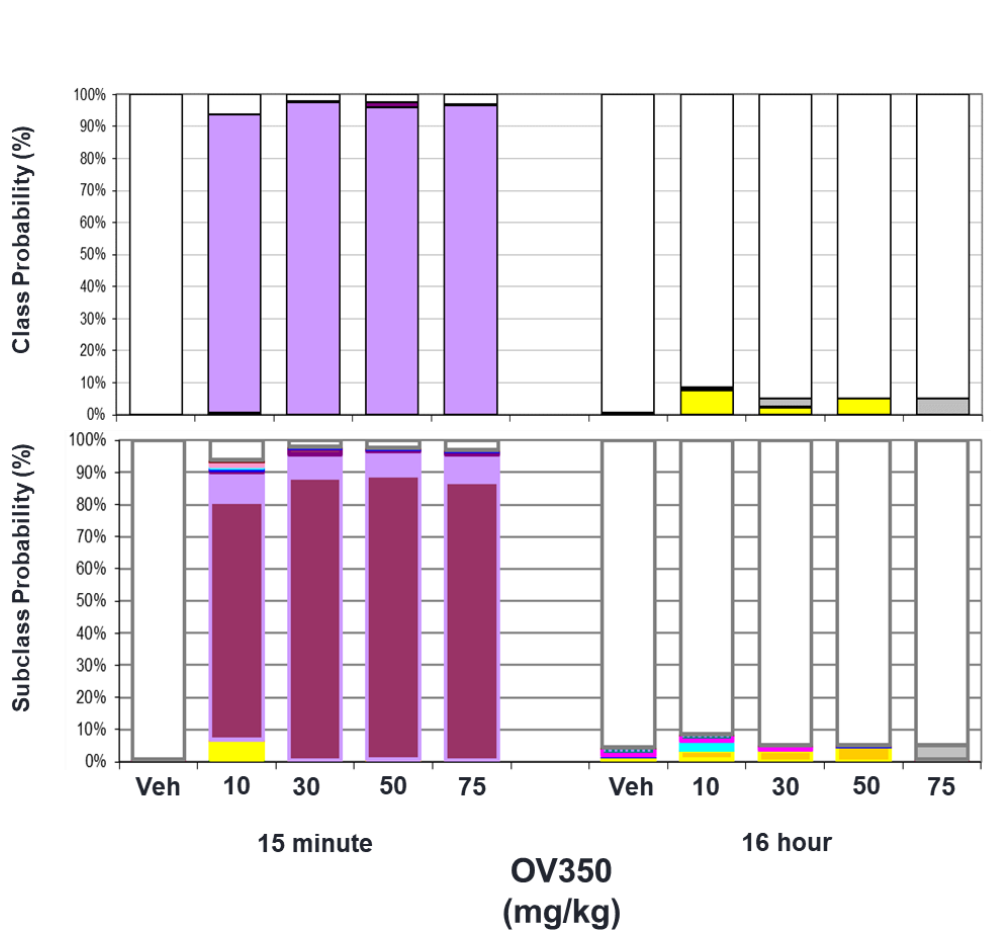
Potent, robust, rapid and reversible antipsychotic activities have been observed for OV350[1]

Behaves as atypical antipsychotic with a clean profile in SmartCube®

Elicits its in vivo effects within 15 minutes of administration

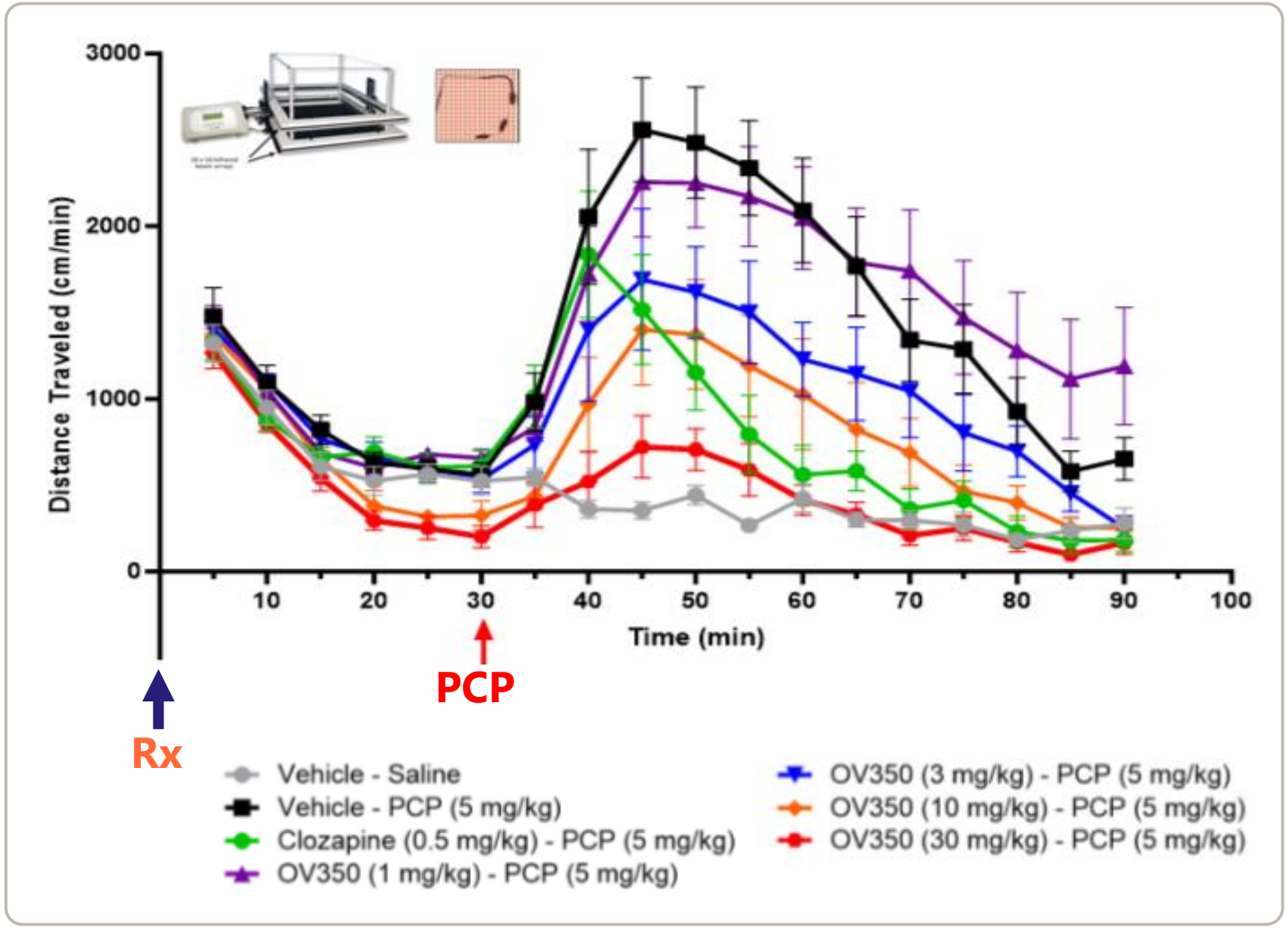
Effects are robust from 10mg/kg dose and increase with higher dose; and disappear in 16 hours

No sedation or other adverse behavior effects observed up to 75mg/kg



1. Ovid data on file

OV350 demonstrates anti-psychotic effects in a schizophrenia model



Phencyclidine-induced psychosis (PCP) is characterized by:

- Confusion, excitation, aggression, paranoia, hallucinations, and can be experimentally measured by hyperlocomotion

OV350 demonstrated dose dependent responses and inhibited PCP induced hyperlocomotion

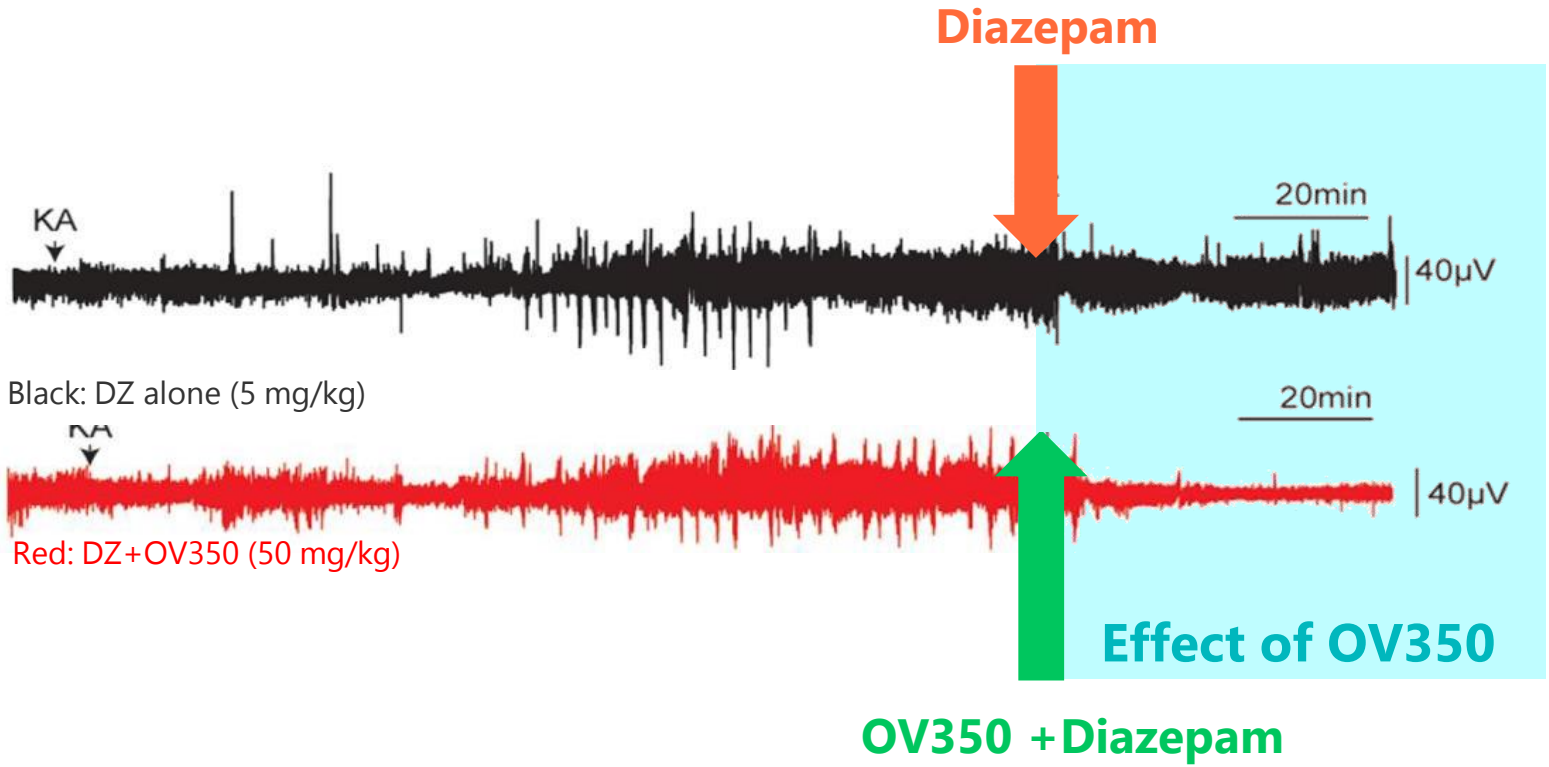
OV350 appears to have anxiolytic effects without causing sedation

1. Ovid data on file

OV350 reduced refractory seizures in diazepam-resistant model

Induction of Status Epilepticus (SE)

EEG traces show SE cessation after OV350 intervention with Diazepam



- Mice implanted with electrodes to measure kainate-induced seizures
- Drug given 2hrs after onset of status epilepticus
- Restored effect of diazepam at high and low doses

1.Jarvis et al., 2023, Cell Reports Medicine 4, 100957
2. Ovid unpublished data

OV350 IND-enabling studies show favorable toxicology profile & dose-dependent exposure

All IND-enabling studies completed

NOAEL identified in both species

Supportive of Phase 1 study

- OV350 exhibits dose dependent exposure
- Ames and in vitro mutagenesis tests negative (i.e., clean)
- DDI assessment completed with no concerns
- Drug product manufacturing on track

Rat (QD)

- Mild, reversible clinical tox observed with no macro/microscopic findings at target dose range
- Cmax and AUC increase dose proportionally

Beagle Dog (QD)

- Well tolerated within target dose range
- No target organ macro/microscopic findings

OV888/GV101

A highly selective ROCK2 inhibitor for potential treatment of cerebral cavernous malformations & other neurovascular disorders

Overview ROCK2 inhibition: OV888/GV101

Collaboration with Graviton Bioscience to realize ROCK2 inhibition for the CNS disorders

OV888, best-in-class potential

- Potent and highly selective for ROCK2
- Well characterized safety profile (two Phase 1 studies)
- Blood-brain barrier penetrant
- Safety profile and tolerability well-characterized in humans (two Phase 1 studies completed)

Novel mechanism

- ROCK2 is a signaling pathway that acts on actin cytoskeletal processes, cellular to extracellular matrix adhesion and fibrosis
- Relevant for conditions with endothelial dysfunction & neurovascular disorders, including cerebral cavernous malformations

Regulatory precedent

- Prior ROCK2 approvals (Rezurock® in GVHD)
- Potential to leverage orphan and/or accelerated approval programs

OV888's potential as a potent, selective, best-in-class ROCK2 inhibitor

	ROCK2 IC_{50} (uM)	ROCK1 IC_{50} (uM)	Selectivity (ROCK1/ROCK2)	BBB Penetrant	Off-Target Effects	Indication
OV888 OVID/GRAVITON	**0.002-0.02**	**12.1**	**1071 fold**	✓		**CCM, and other undisclosed indications**
KD025[1] Kadmon Pharmaceuticals	0.105	24	~80 - 100 fold	×		Graft vs host disease
NRL-1049[2] (Neurellis)	0.24 – 0.73	3.9 – 10.2	13.9 – 16 fold	✓	✓	CCM

1. Ann Clin Transl Neurol. 2014 Jan; 1(1): 2–14. Published online 2013 Nov 19. doi: 10.1002/acn3.19
2. https://patents.google.com/patent/US10106525B2/ena
3. (Chart based on biochemical assays; not head-to-head studies)

OV888/GV101 capsule: Phase 1 topline results

Overview

- OV888/GV101 capsule formulation
- Double-blinded, placebo controlled
- Male/female healthy adult volunteers
- 7-day consecutive dosing:
  - MAD: 100 mg, 200 mg, 400 mg, and 600 mg
- Objective to measure:
  - Safety
  - Tolerability
  - Pharmacokinetics

Results

- ✓ Objective met: Well-tolerated at all tested doses
- ✓ Target engagement achieved
- ✓ Exposure & half-life supportive of once daily dosing
- ✓ Results:
  - No SAEs; no participants met preset stopping criteria
  - All AEs were mild and resolved
  - Asymptomatic laboratory results rated grade 2 or higher in at least 5% of subjects:
    - Clinically insignificant increases in total bilirubin without direct hyperbilirubinemia, with no concurrent liver enzyme elevations, reported in 30% of participants
    - Creatine phosphokinase elevations without muscle pain or weakness were reported in 7% of participants
    - All participants normalized during the study period

Source: Ovid & Graviton data on file

Clinical development status: OV888/ GV101

Completed Phase 1 safety study

- Target engagement demonstrated in humans
- No serious adverse events, well tolerated at all doses tested

Phase 2 trial initiation in CCM on pause

- Secured regulatory approval to proceed with patient dosing
- Paused to evaluate insights from recently completed competitor trials in CCM, including:
  - Results, duration, biomarkers, enrichment strategies

With Graviton, continuing to explore additional indication opportunities

Thank you