OV329: Next generation GABA-AT inhibitor

Julia Tsai, PhD

Senior Vice President, Head of Epilepsy & Clinical Development and Medical Affairs

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OV329 shows efficacy in multiple animal models & encouraging safety profile

- Effective in multiple acute and chronic animal models of epilepsy/seizures
- Preclinical data suggest potential for promising safety profile compared to 1st generation GABA-AT inhibitors
- On-track for IND submission and to be in the clinic later this year

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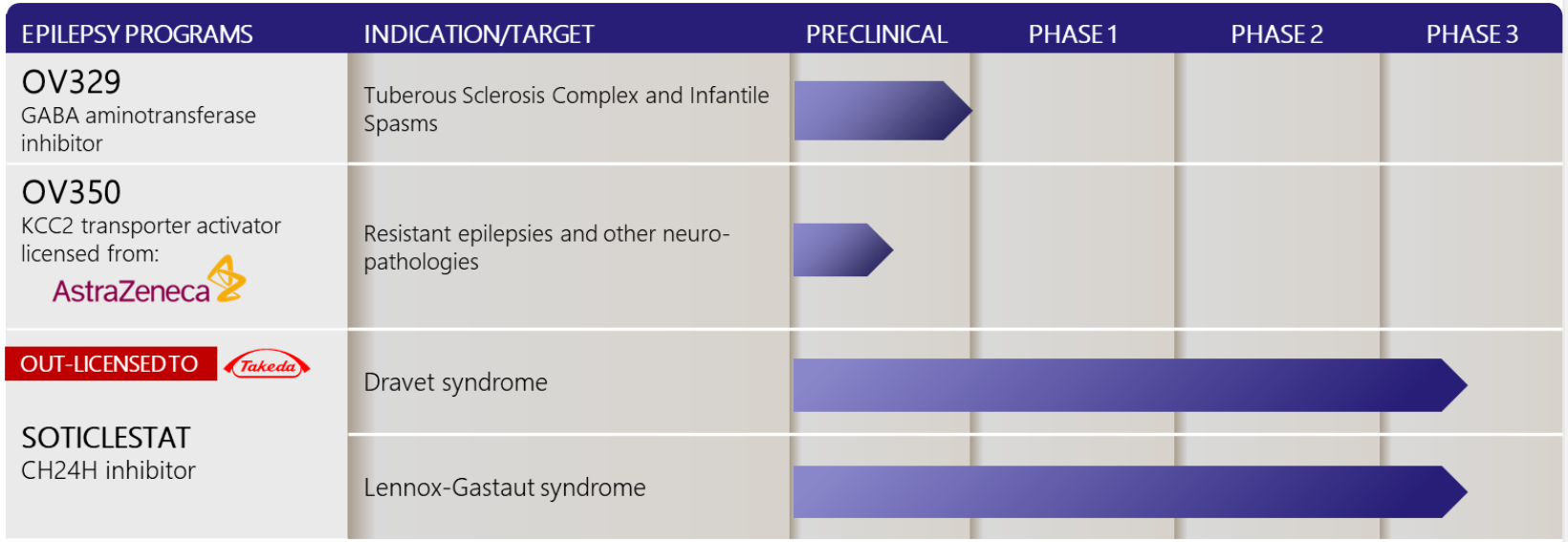
Ovid Therapeutics

Vision: Conquer epilepsies & brain disorders with courageous science

- 2 preclinical programs with potential 1st-in-class or best-in-class medicines
- Novel mechanisms of action for the potential treatment of epilepsy
- Out-licensed novel cholesterol 24-hydroxylase inhibitor to Takeda
- Preclinical pipeline targeting genetic epilepsies and seizures



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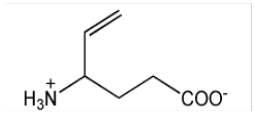
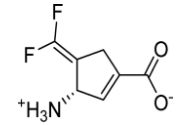
OV329 is a potent, next-generation GABA-AT inhibitor

- Potential candidate for treatment of drug-resistant epilepsy
- Well-characterized target
- Similar mechanism of action to vigabatrin
- More potent than vigabatrin
- Potentially improved safety profile

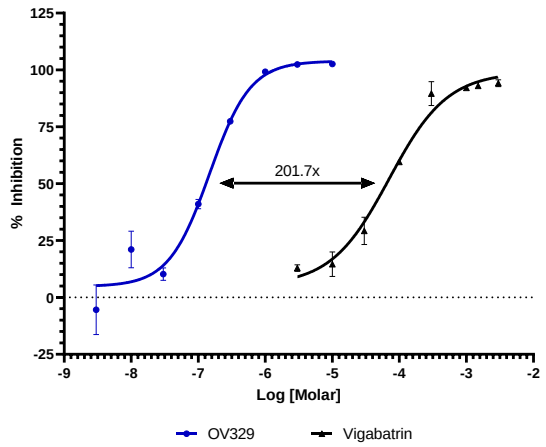
Vigabatrin



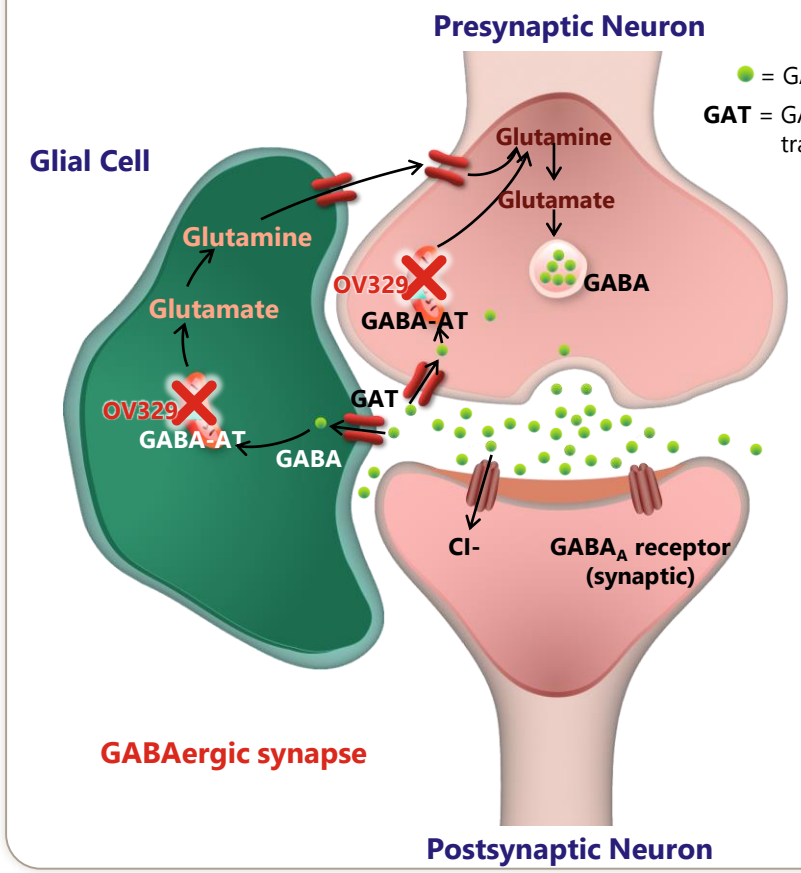
OV329



GABA Amino Transferase Assay (Rat Brain)



OV329 facilitates GABA transmission



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OV329 is active in suppressing seizures in multiple animal models, including drug-resistant models

	Model	Injury Model	Clinical Correlate	Species	Dosing	OV329 Activity (seizure protection)
	6 Hz Electrical Stimulation	Acute/seizure	Acute focal to bilateral tonic-clonic seizure	Mouse	Acute (0.01, 0.1, 0.3, 1 mg/kg/day, p.o.)	–
	Maximal Electroshock (MES)	Acute/seizure	Generalized tonic-clonic seizure	Mouse	Acute (1, 3, 10, 30 mg/kg, p.o.)	–
Presented today	**i.v. Pentylenetetrazol (ivPTZ)**	**Acute/seizure**	**Nonconvulsive seizures (eg absence, myoclonic)**	**Rat**	**Acute (5, 20, 40 mg/kg i.p.)**	+
	NMDA-Induced Infantile Spasm Model	Acute/seizure	Infantile spasms	Mouse	Acute (0.0025, 0.01, 0.1, 1 mg/kg, p.o.)	+
	Audiogenic Seizure	Acute	Generalized seizures	Mouse	Acute (0.01, 0.05, 0.1 mg/kg, p.o.)	+
Presented today	**Amygdala Kindled**	**Chronic/epilepsy**	**Chronic focal to bilateral tonic-clonic seizure/ pharmacoresistant seizures**	**Rat**	**Acute (30, 40 mg/kg, i.p.)**	+
	Intrahippocampal Kainate Model of Mesial-Temporal Lobe Epilepsy (MTLE)	**Chronic/epilepsy**	**Mesial temporal lobe epilepsy/ pharmacoresistant seizures**	**Mouse**	**Acute, single dose (0.01, 0.1, 1, 10 mg/kg, p.o.; 10mg/kg, i.p.)**	+

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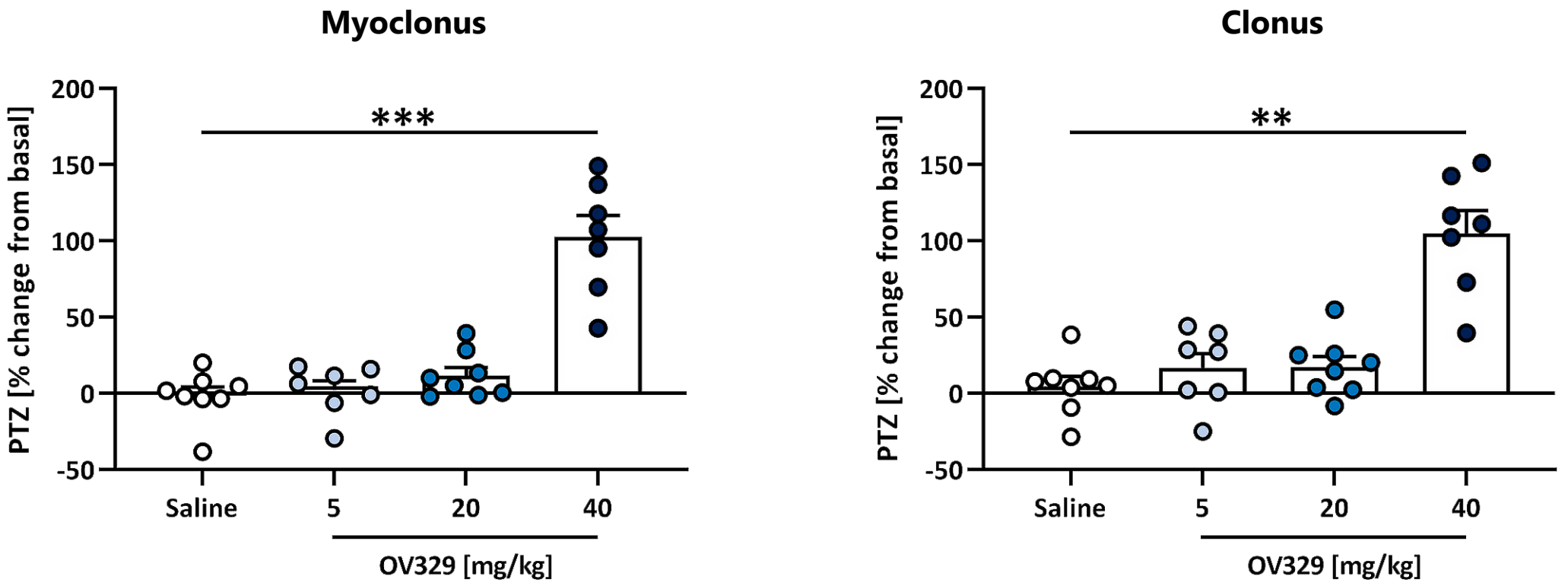
OV329 has anticonvulsant effects in the ivPTZ-induced rat seizure model

OV329 dose-dependently increases the thresholds of ivPTZ-induced seizures



*Treatment effects calculated as percent change from basal seizure thresholds
Data are expressed as mean + SEM, **p<.01; ***p<.001

Feja et al, Epilepsia, 2021;00:1-14.

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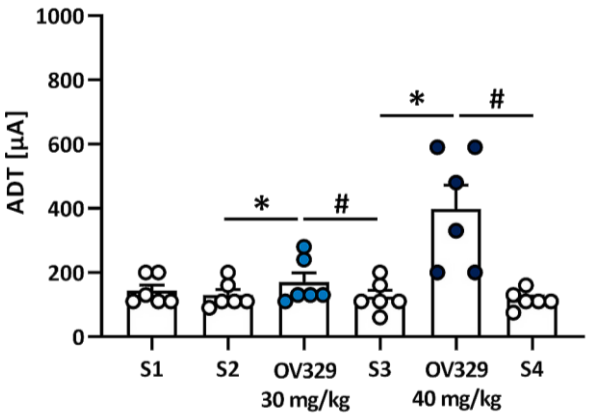
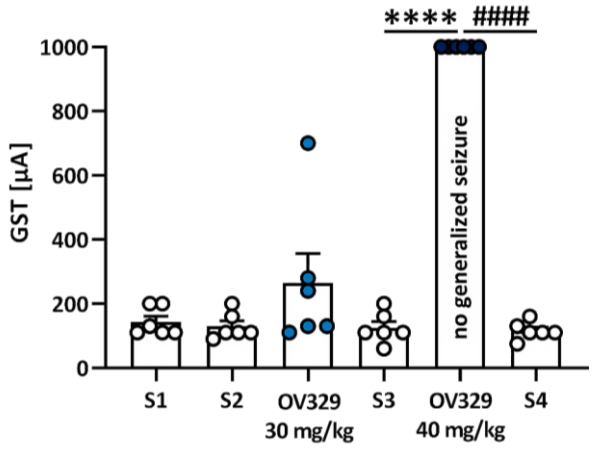
OV329 has anticonvulsant effects in the amygdala-kindled rat model

OV329 increases the afterdischarge threshold, suppresses generalized seizures, and reduces seizure severity in amygdala-kindled rats

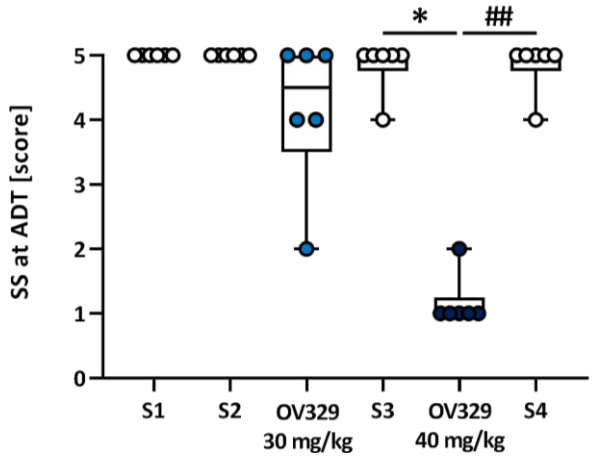
Afterdischarge threshold (ADT)



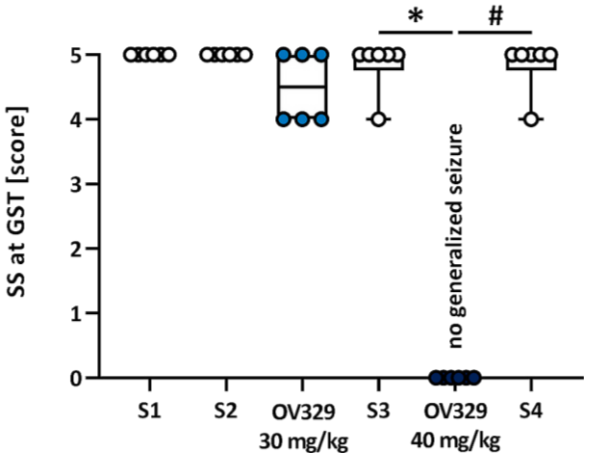
Generalized seizure threshold (GST)



Seizure severity (SS) at ADT



Seizure severity at GST



*p<.05, **p<.01, ***p<.001
S1-S4: pre- and post-drug saline controls

Feja et al, *Epilepsia*, 2021;00:1-14.

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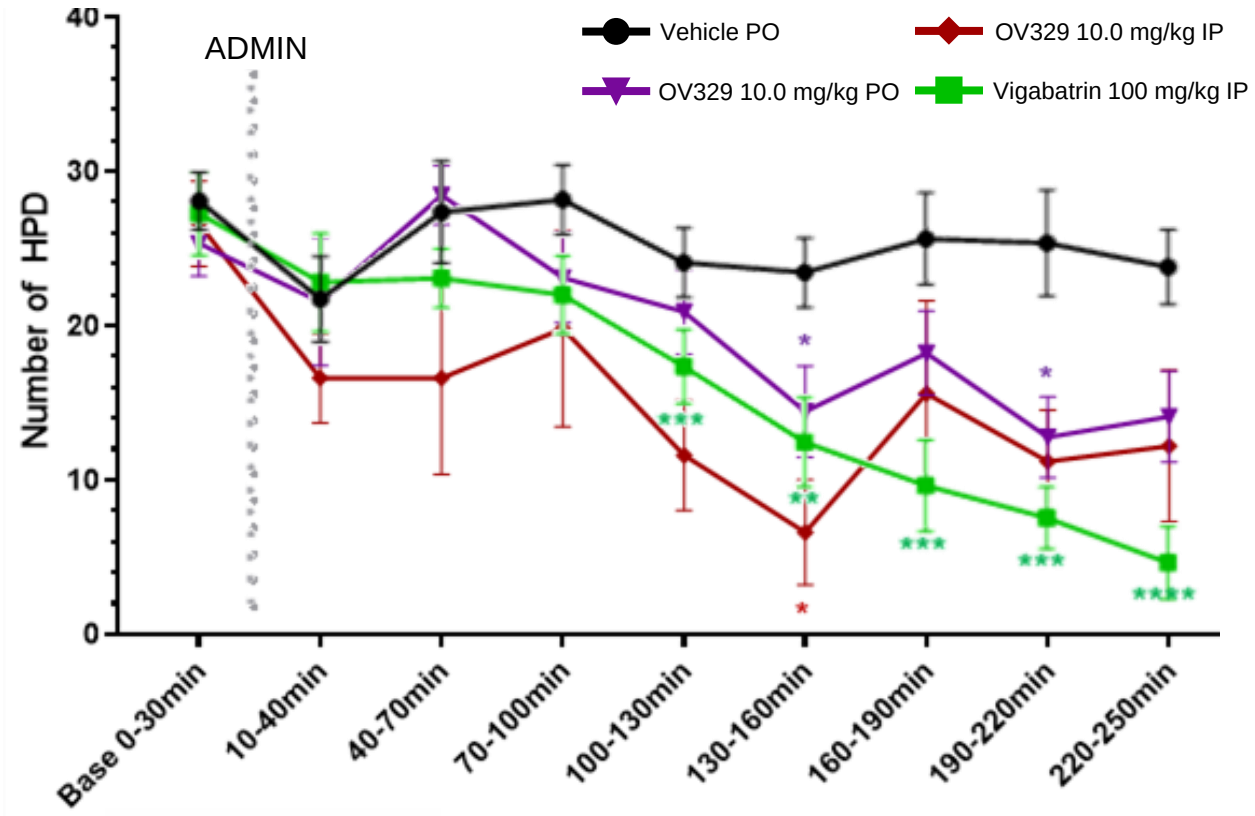
OV329 has anti-seizure activity in mesial-temporal lobe epilepsy mouse model of drug resistant epilepsy



- 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

Results

Single-dose OV329 significantly suppressed the number of focal seizures in the MTLE mouse model

[1]Duveau, et al. *CNS Neurosci Ther*. 2016;22(6):497-506; [2]Sarmiere, PD et al. *American Epilepsy Society Meeting*, 2021.

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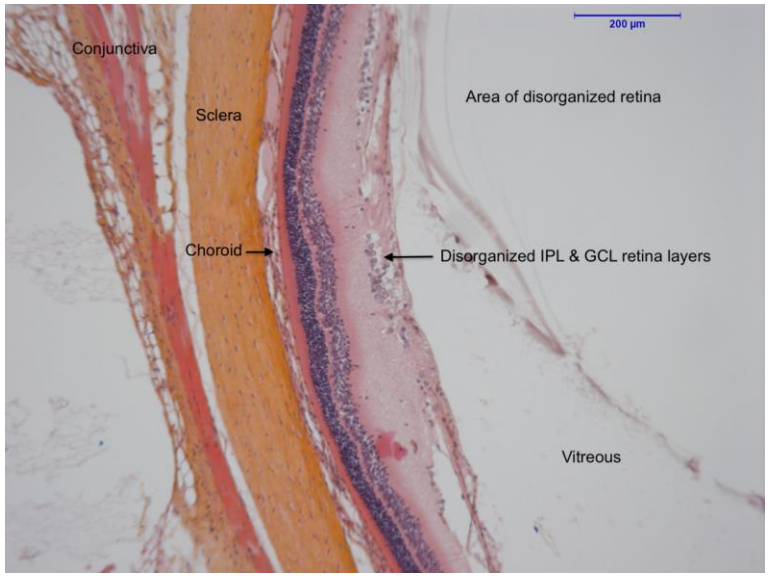
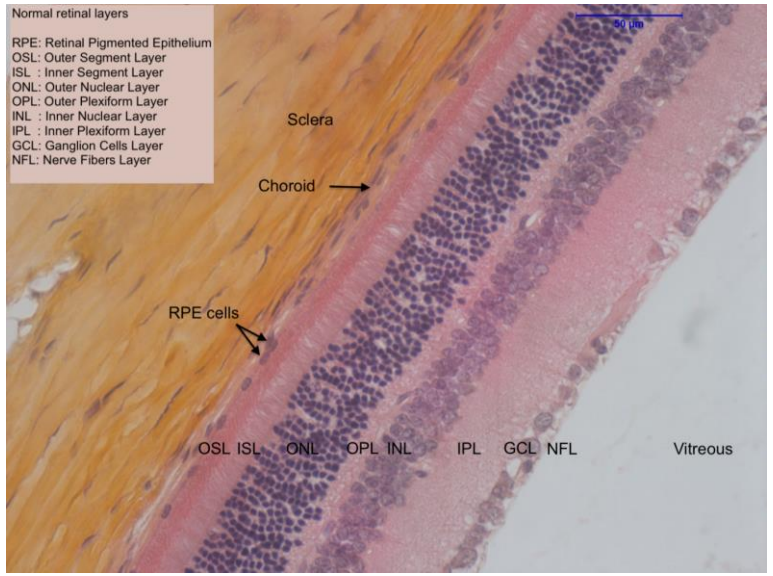
No ocular effects seen following chronic exposure with OV329 (3 mg/kg)

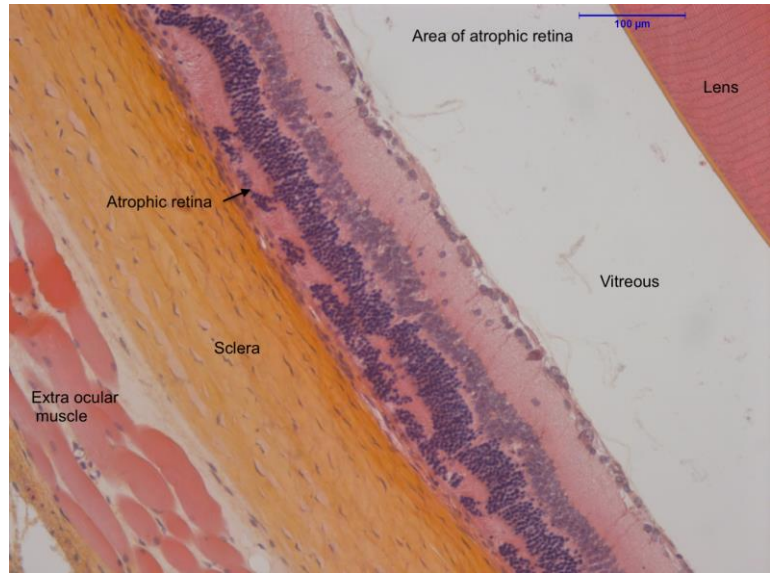
Vehicle
Animal R76



OV329 3.0 mg/kg
Animal R13



Vigabatrin 300 mg/kg
Animal R91



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

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

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OVID, *Data on file*

Summary: OV329 demonstrated anti-seizure activity at tolerated doses in multiple animal models

- OV329 is a next-generation GABA-AT inhibitor in development as an anti-seizure medication for rare adult and pediatric epilepsy disorders
- Non-clinical studies have demonstrated anti-seizure activity of OV329 in multiple seizure models, including drug-resistant animal models
- Safety profiles established in mice, rat and canine models:
  - Initial preclinical safety studies suggest OV329 was well-tolerated up to 3.0 mg/kg/day and no ocular signals were observed at these doses
  - Repeat-dosing studies at 3.0mg/kg/day in efficacy models are ongoing
- Planning IND submission and Phase 1 initiation in 2H, 2022

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