Ovid Therapeutics

Corporate presentation

November 10, 2026



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Forward-looking statements

This presentation includes certain disclosures by Ovid that contain "forward-looking statements" including, without limitation: statements regarding the reproducibility and durability of any favorable results initially seen to date in clinical trials; the potential therapeutic and market opportunity of OV329, OV4071 and other compounds from Ovid's library of direct activators of KCC2; the expected timing of initiation, completion, and results and data of Ovid's ongoing and planned clinical studies; Ovid's expectations regarding the duration of its cash runway and the expectation that it will support Ovid's operations and development programs; the potential use and development of OV329, OV4071 and other compounds from Ovid's library of direct activators of KCC2; Ovid's clinical pipeline strategy and plans for future clinical studies; the potential future indications for OV4071 and other compounds from Ovid's library of direct activators of KCC2; and other statements that are not historical fact. You can identify forward-looking statements because they contain words such as "anticipates," "believes," "expects," "intends," "may," "plan," "potentially," and "will," and similar expressions (as well as other words or expressions referencing future events, conditions or circumstances).

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Developing potential best-in-category medicines to manage conditions caused by neural hyperexcitability

Fundamental biological targets

Pursue targets with extensive evidence for quelling excess neural hyperexcitability

Differentiated, universal mechanisms of action

Ensure MOAs with broad therapeutic utility can stand apart in a crowded field

Better, gentler medicines

Leverage medicinal chemistry & discovery capabilities to design bespoke programs

Culminating in a fully integrated neurotherapeutics company
with multiple, sequential clinical & regulatory milestones

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Clinical pipeline of differentiated small molecule medicines

Potential indications		Preclinical / Phase 1 / Phase 2	Anticipated milestones*
OV329, a next-generation GABA-aminotransferase inhibitor			
Drug-resistant adult focal epilepsy (FE)	Novel mechanism of action in FE targeting: • Competitive efficacy profile • Superior tolerability & safety profile • No expected titration or drug:drug interactions	**Phase 2 RCT** **Open label photo paroxysmal response PoC initiated**	• Phase 2 initiated; data in H2 2027 • Open-label photo paroxysmal response (PPR) initiated; data in Q1 2027
Tuberous sclerosis complex seizures (TSC)	Potential 1st approved GABA-AT inhibitor • Preferable safety, tolerability profile • Increased treatment duration	**PoC & safety**	• PoC safety and signal-finding study to initiate in Q4 2026
Infantile spasms (IS)	Potentially disease-modifying 1st line agent • Preferable safety, tolerability profile • Increased treatment duration	**PoC & safety**	• Infant formulation and enabling studies ongoing; open label safety and signal-finding study planned for 2027
OV4071, potassium-chloride cotransporter 2 (KCC2) direct activator (oral)			
Broad spectrum psychosis	• Acute schizophrenia Additional indications: • Neurodegenerative psychoses • Other undisclosed indications	**Phase 1** **Ketamine study**	• Phase 1 proof-of-mechanism ongoing; data in Q1 2027 • Ketamine study data in Q1 2027 • Phase 2 schizophrenia study planned for 2027

*Timelines pending feedback from regulatory discussions Ketamine challenge to initiate pending PK characterization in Phase 1 study

Additional undisclosed KCC2 development candidates from unique direct activator portfolio

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OV329

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OV329: A unique validated mechanism for a significant epilepsy market

Crowded market and unmet need remains

Large, underserved population
1.2M U.S. adults with drug-resistant epilepsy; many on 2+ ASMs

Current ASMs fall short
Seizures persist and CNS side effects are often unmanageable

Epilepsy isn't "winner-take-all"
Vigabatrin's safety limits use; demand for new options persist

How OV329 competes

Robust seizure control
Potent target engagement, positive Phase 1 PD data

Rationally designed for improved tolerability
No anticipated sedation or retinal accumulation

Simplified treatment
Low-dose, no titration and combinable

Broad therapeutic potential
A more tolerable GABA-AT inhibitor for FE and DEEs including TSC and IS

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OV329 designed to replace first-generation GABA-AT inhibitor, vigabatrin

Vigabatrin had proven efficacy, but was hampered by compound-specific safety concerns

Indications	VGB efficacy	VGB safety
Focal epilepsy	40% or greater reduction in FE frequency[1]	Used as a last-line only treatment due to ophthalmic safety
TSC-associated seizures	Responders >90% seizure reduction[2] 46% seizure freedom frequency[2]	Limited to short treatment duration due to safety
Infantile spasms	Freedom from spasms ~47%[2] Freedom from treatment failure ~37%[2]	Limited to short treatment duration due to safety

1. FDA Medical Review(s) for Sabril (vigabatrin), 2009, U.S. Food and Drug Administration.
2. Vigabatrin historical data

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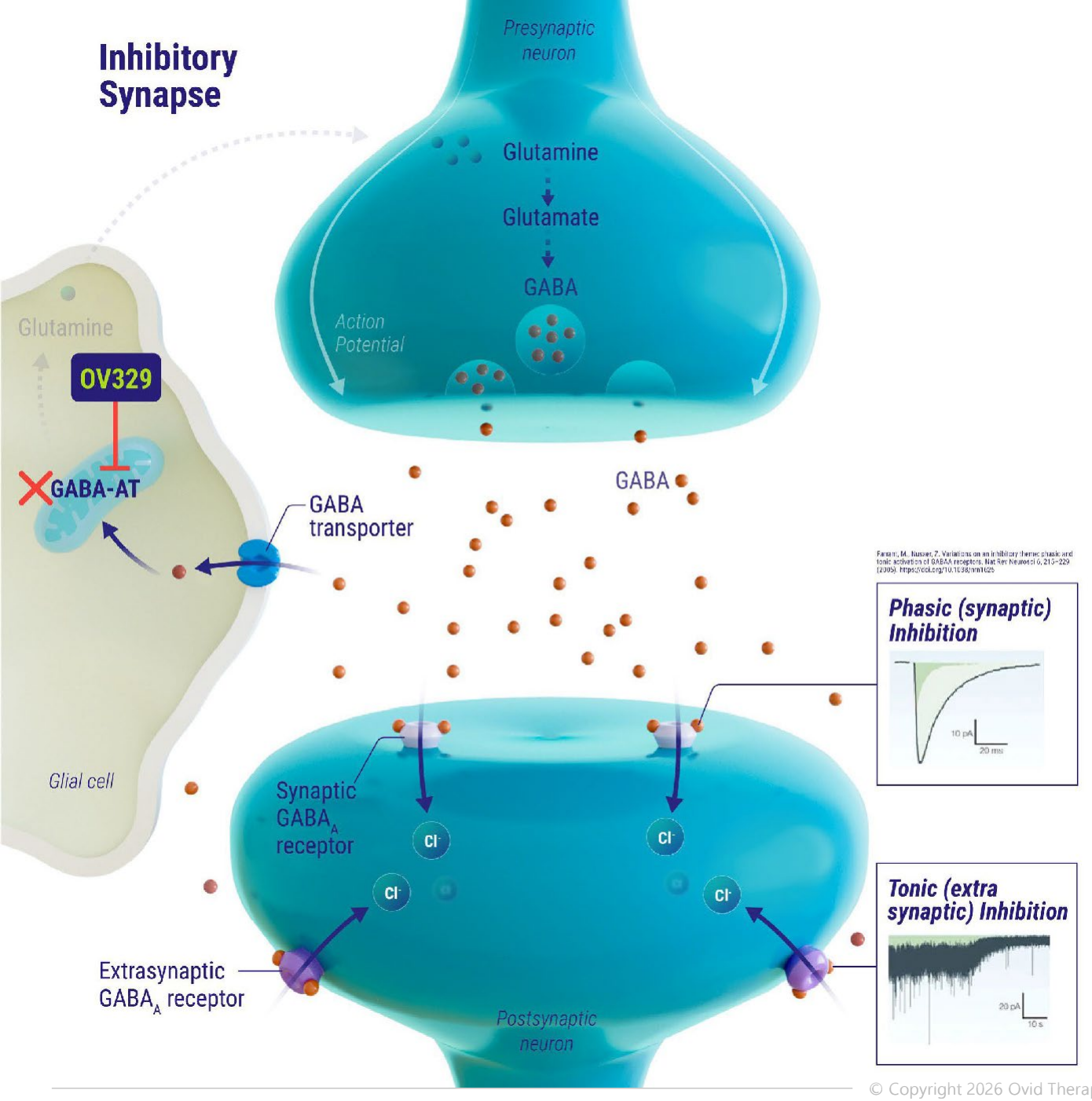

GABA-AT inhibition: Proven MOA to reduce neural hyperexcitability & seizures

OV329 believed to optimally tune GABA to enhance tolerability & efficacy

Inhibits GABA-AT, enzyme that degrades inhibitory neurotransmitter, GABA[1]

Increases GABA in synapse & extra-synaptic regions delivering phasic & tonic inhibition[2]

Creates inhibitory neural environment that avoids tolerability issues of VGB associated with surging GABA in synapse, including irreversible vision loss

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. Colmers P et al. eNeuro 27 June 2024, 11 (7) ENEURO.0137-24.2024; https://doi.org/10.1523/ENEURO.0137-24.2024

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OV329: A substantial franchise for adult epilepsies and DEEs

Potential indications & U.S. prevalence

Adult epilepsy opportunity

Treatment-resistant focal epilepsy*	**~0.5-0.7M[1]**

Active DEE opportunities + expansion

TSC-associated seizures*	**~30-40K[2]**
Infantile spasms*	**~6-8K[3]**
Lennox–Gastaut syndrome	**~40-50K[4]**
CDKL5 deficiency disorder	**~1.8K[5]**
Focal Cortical Dysplasia	**~3.2K[6]**

Unique formulation

Adult fixed-dose tablet

Pediatric granules

Weight-based, flexible dosing

U.S. opportunity

Adult FE opportunity

>$1B

Large established refractory epilepsy market

Pediatric DEE opportunity

>$1.5B

Expansion opportunity across rare DEEs

Pediatric granules support distinct orphan-drug positioning

***Programs actively being pursued by Ovid**

1. CDC/Kobau et al. Epilepsy & Behavior (2023
2. TSC Alliance (2024), Furber et al. (2025)
3. Go et al. Neurology (2012)
4. LGS Foundation (2024)
5. Liogier d'Ardhuy et al. Epilepsia (2026)
6. Lopez-Rivera et al., Epilepsy & Behavior Reports (2022)

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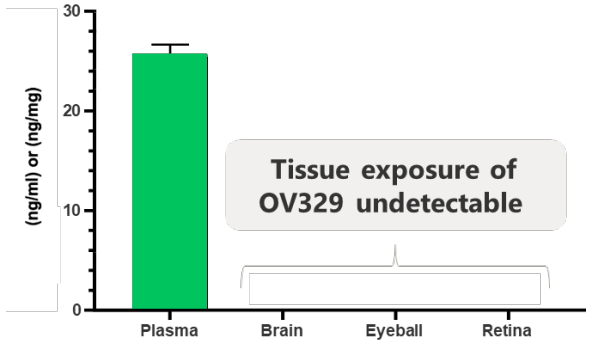
OV329 does not accumulate in the retina, in contrast with VGB

No accumulation of OV329 detected inthe eye or retina, whereas vigabatrin accumulates*[1,2]

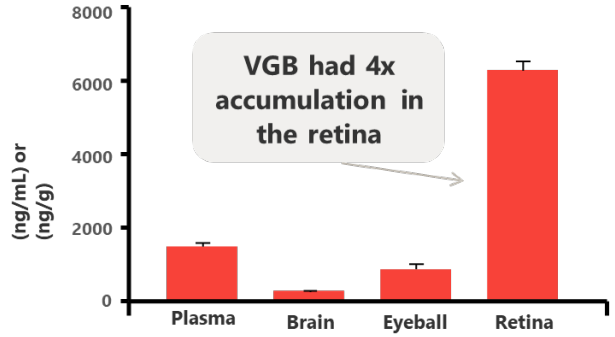
OV329

Mean Plasma and Tissue Concentration 5.0 mg/kg/day

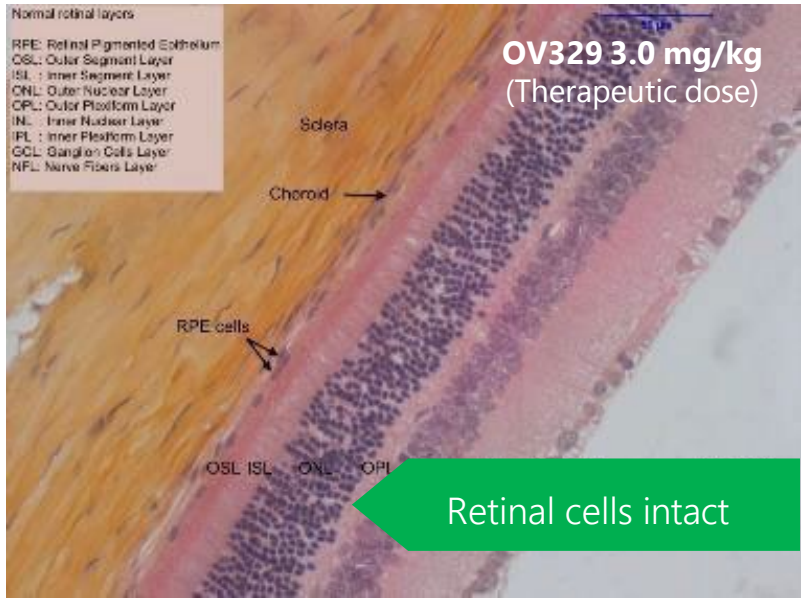


VIGABATRIN

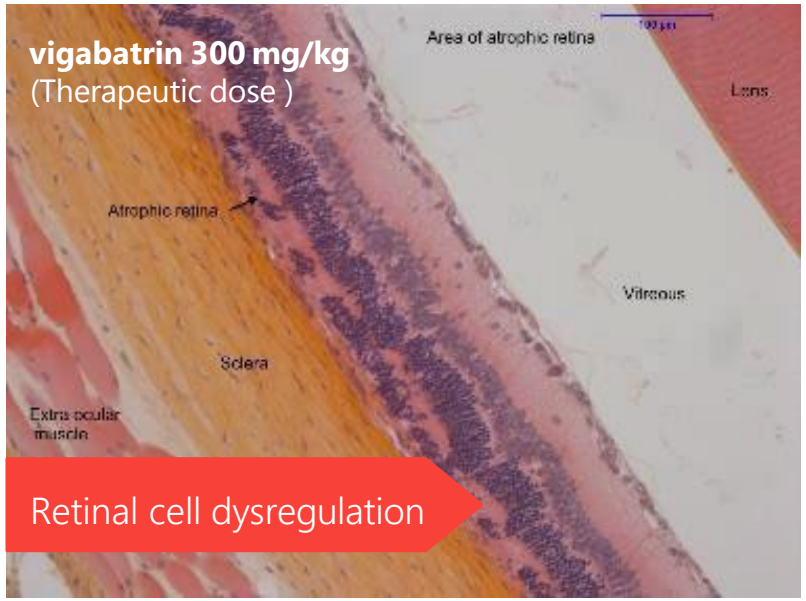
Mean Plasma and Tissue Concentration at 80.0 mg/kg/day



VGB shown to cause retinal cell dysregulation in < 45 days, OV329 shows no ocular effects[1]



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



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

Dedicated ophthalmic safety studies of OV329 conducted in mice, rats, humans

*OV329 gets into the brain and irreversibly binds to the GABA-AT enzyme

1. Zhong, 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
2. Walters et al. Pharmacol Res Perspect. 2019 Jan 7:7(1)
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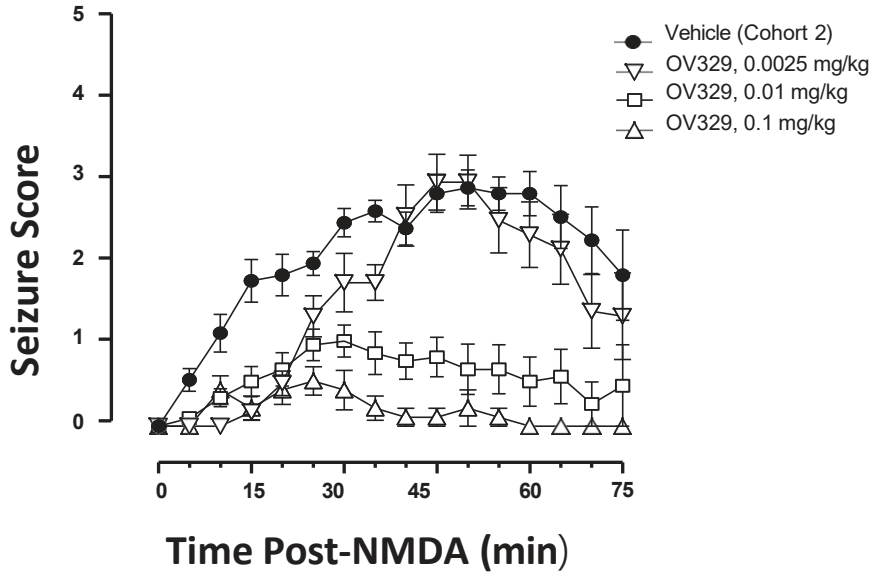
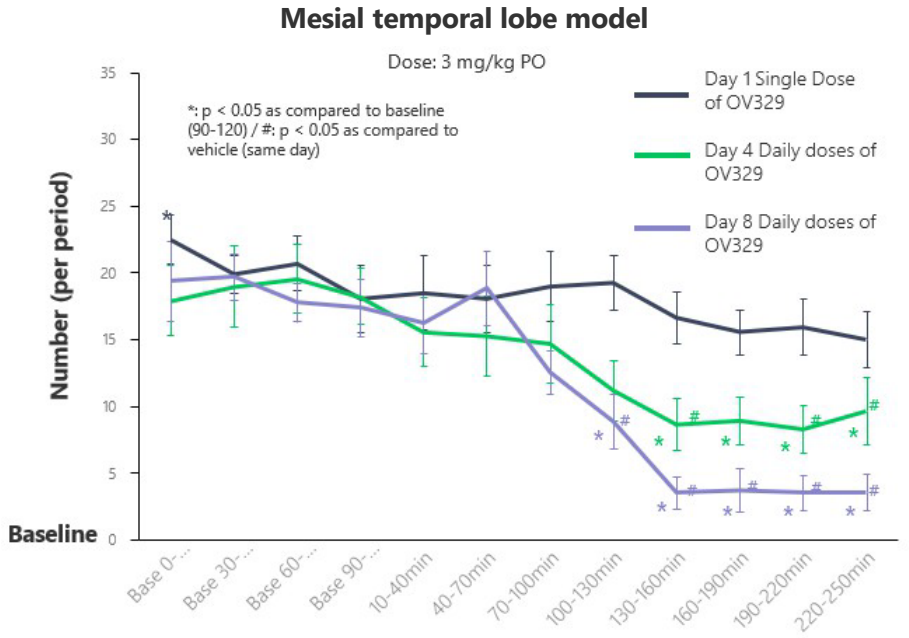
OV329 shows compelling anticonvulsant effects in infantile spasms, focal and broad seizure models

OV329 reduced seizure score in a mouse model of infantile spasms even at low doses[1]



Repeat, low doses reduce seizure frequency & duration in animal models of focal seizures[2]



Anti-convulsant efficacy demonstrated in 9 additional seizure models

1. Ovid data on file
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.

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OV329 Phase 1 trial demonstrated potential best-in-class safety profile, with no ophthalmic or retinal changes

No treatment-related serious adverse events at any dose

Dose	Adverse event	OV329	PBO	Severity	Drug related	Outcome
2 mg MAD	Headache	n=1	n=0	Mild (grade 1)	Possibly related (×2)	Recovered or resolved (×2)
2 mg MAD	Drowsiness	n=1	n=0	Mild (grade 1)	Possibly related	Recovered or resolved
5 mg MAD	Metallic taste	n=1	n=0	Mild (grade 1)	Related	Recovered or resolved
7 mg MAD	None	None	n=0	N/A	N/A	N/A
9 mg MAD	None	None	n=0	N/A	N/A	N/A

No treatment-related ophthalmic effects

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

Supportive safety profile at all doses · 5 mg and 7 mg reach exposure predicted to be anti-convulsant

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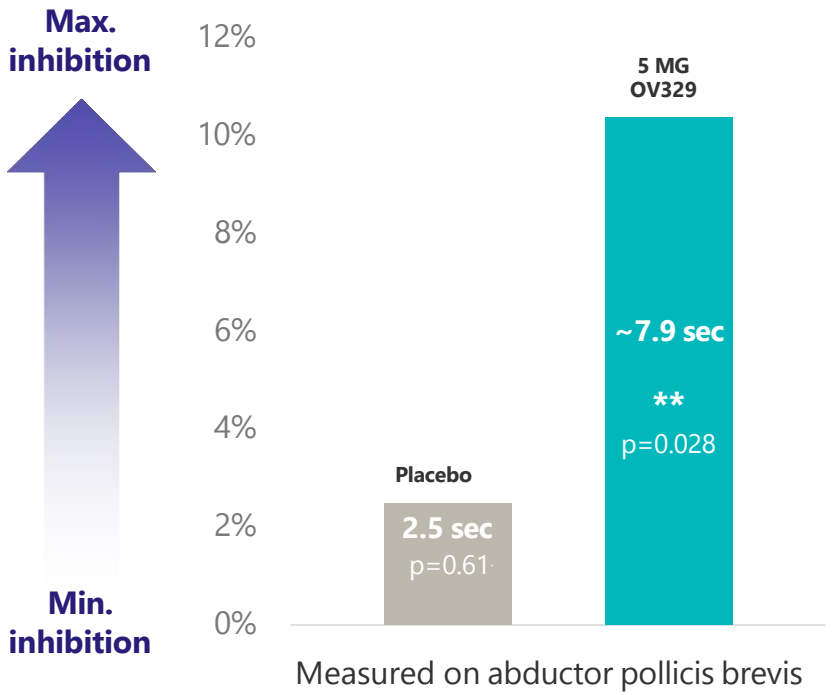
OV329 Phase 1 trial demonstrated dose dependent GABA elevation & cortical inhibition

OV329 increases inhibition as measured by the cortical silent period (CSP)

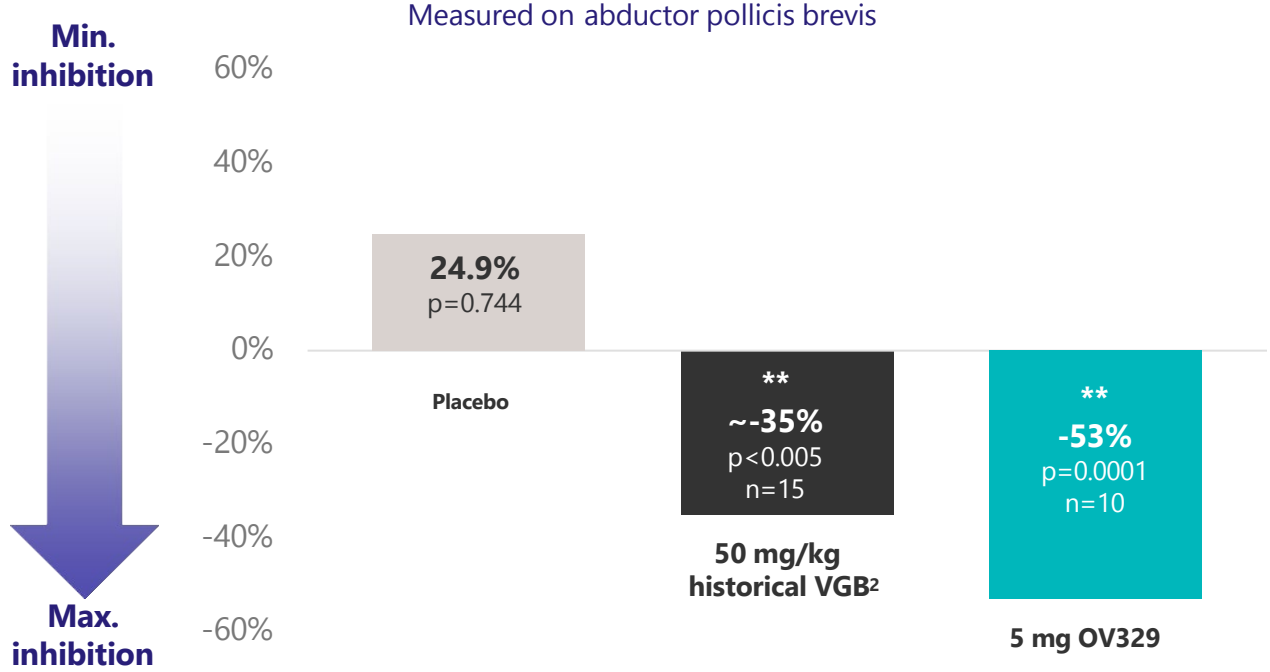
Untreated baseline vs post-treatment on day 7



Significantly increased cortical inhibition exceeding vigabatrin's inhibition

Long-interval cortical inhibition (LICI) 150 ms change: Undrugged baseline vs post-treatment on day 7[1,2]

Measured on abductor pollicis brevis



Note: Information compares similar studies and methodologies; a head-to-head trial was not conducted

Baseline is at Day 1 prior to any treatment

Pierantozzi et al., Brain Res. 2004 Nov 26; 1028(1):1-8

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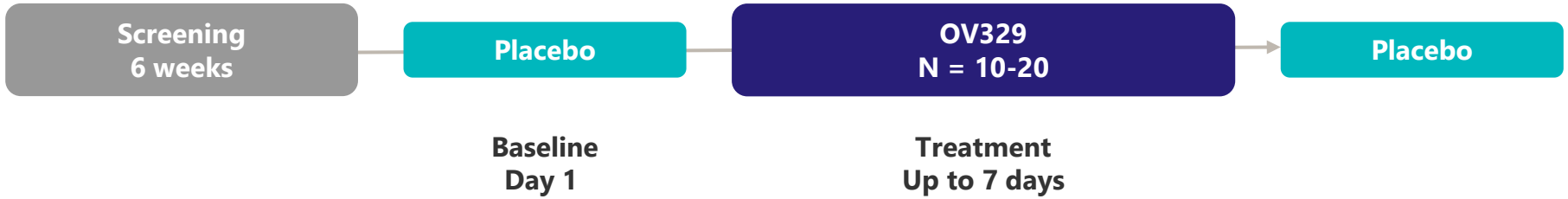
Photoparoxysmal EEG response (PPR) trial design

Randomized, placebo-controlled study in participants with photosensitive epilepsy



Objective

- Demonstrate target engagement using an objective and sensitive measure in patients

Design

- Global, placebo-controlled, single-blind proof of concept study
- Robust PPR assessments on several timepoints over multiple days
- Adult participants with reproducible PPR induced by intermittent photic stimulation (N=10-20)
- 7 mg once daily dosing. Additional dose cohorts (5 mg and 9 mg)
- PPR assessments conducted after acute dosing (1 day) and repeated days of dosing (up to 7 days)

Key endpoints

Primary

- Change from baseline in standardized photoparoxysmal response(SPR) after acute and repeated doses

Secondary

- Incidence and severity of treatment-emergent adverse events, PK/PD relationship for OV329 and PPR

PD=pharmacodynamic; PK=pharmacokinetic; SPR= standardized photoparoxysmal response

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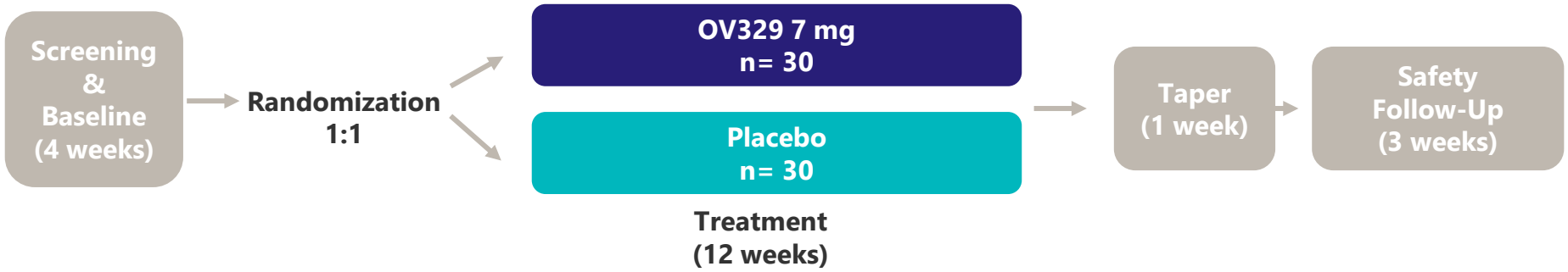
Phase 2 focal epilepsy trial design

Global, multi-site, randomized, double-blind, placebo-controlled adjunctive study in refractory adult focal epilepsy



Objective

- Assess safety, tolerability, efficacy, & PK

Eligibility

- 18-65 years old
- Drug-resistant focal epilepsy for ≥ 2 years
- ≥4 focal seizures per 28 days
- Receiving 1 to 3 anti-seizure medications
- Not currently on vigabatrin

Key endpoints

Primary

- Safety - incidence of TEAEs, clinical labs and vitals, ECGs, ophthalmological exams
- Efficacy - Change from baseline in Primary Focal Seizures (monthly frequency, responder rate), clinical global impression of improvement, PK

Exploratory

- Change from baseline in all seizure types, proportion of seizure-free days, need for rescue medication, exposure-response, quality of life

ECG=electrocardiogram; PK=pharmacokinetic; TEAEs=treatment-emergent adverse events

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KCC2 portfolio

Pioneering KCC2 direction activation

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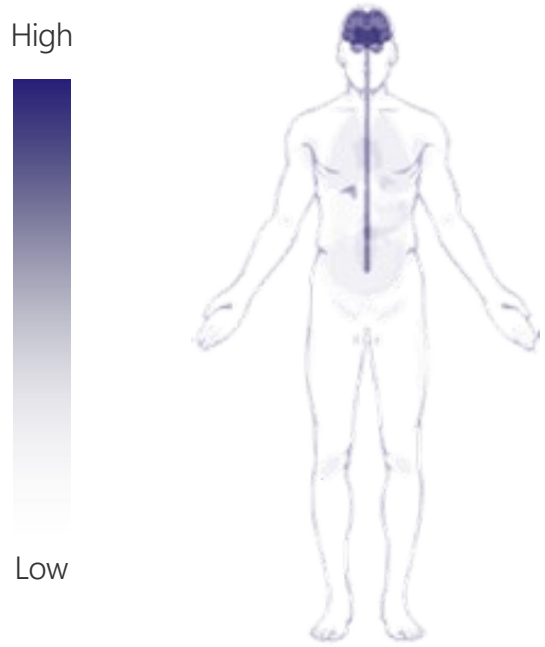
KCC2: A "master switch" for regulating GABA in the brain

Expression exclusive to the CNS
Selective approach activates “brakes” in brain precisely where GABA is underexpressed or dysfunctional

Optimally restores E/I balance
KCC2 is well-positioned upstream of neurotransmitter blockers, but downstream of many causes of hyperexcitability

Nearly impossible to overmodulate
KCC2 acts only when chloride extrusion is sub-optimal, so the gradient is self-limiting

KCC2 exclusively expressed in CNS



Potential across neurodegenerative psychoses/cognition, anxiety/behavioral dysregulation, neurodevelopmental conditions, and pain

E/I: Excitatory/inhibitory

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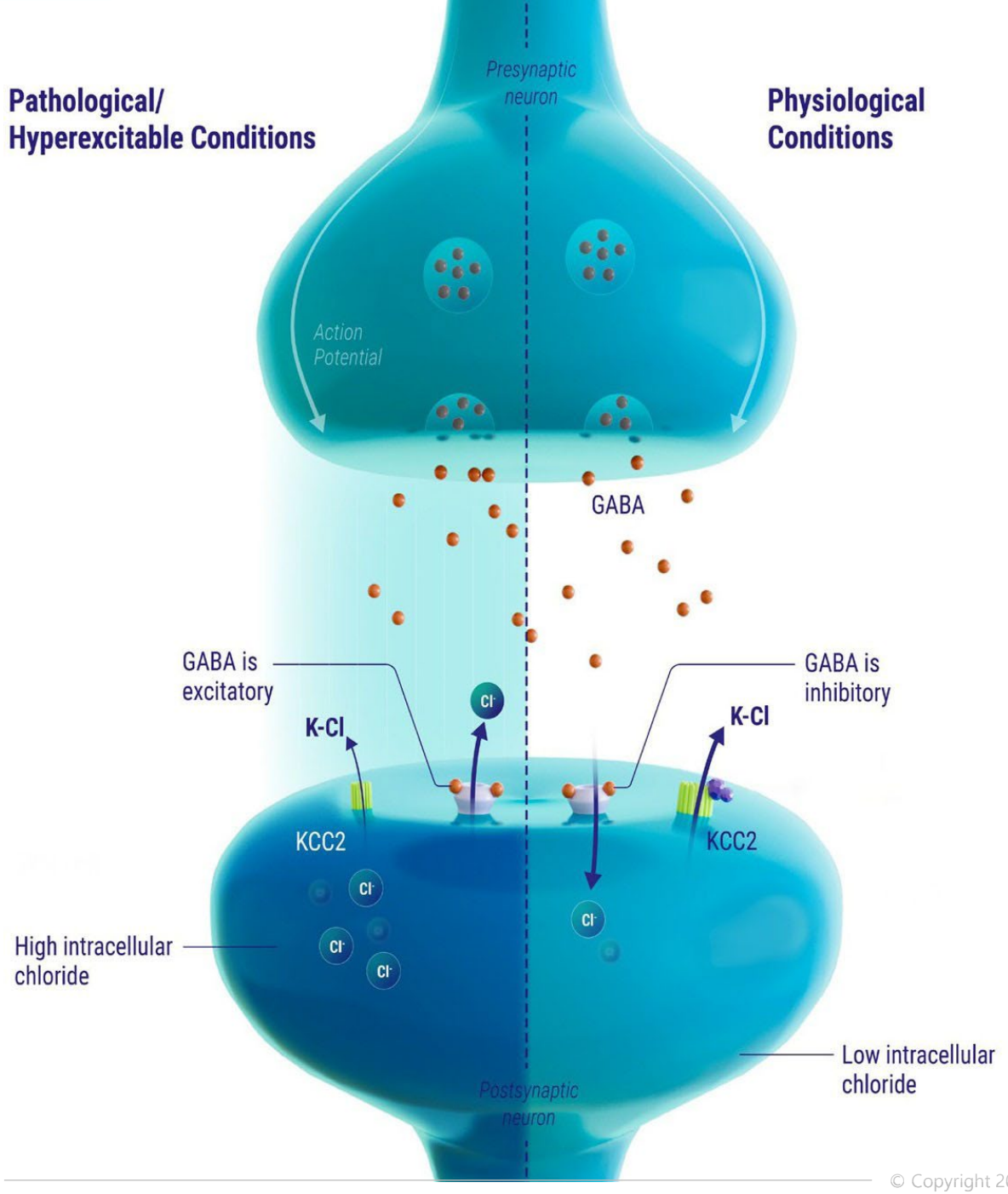

KCC2 is main regulator of GABA inhibition by maintaining neuronal chloride homeostasis

Impaired KCC2 activity causes high intra-neuronal chloride concentrations

Leads to abnormal depolarizing of the GABA receptor

Causes neuronal hyperexcitability

High KCC2 activity leads to low intra-neuronal Cl− concentration

Enables a GABA-driven influx of Cl−, causing an inhibitory effect (hyperpolarizing) to the GABAA current

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Lead candidate OV4071 is a potent, oral KCC2 direct activator

OV4071

- Excellent preclinical safety profile:
  - No off-target activity
  - No sedation or catalepsy
  - No drug:drug interactions anticipated
- Drug properties are highly potent and selective
  - 20-fold potency in psychosis models vs OV350
  - 0.64 µM KCC2 activity
  - Confirmed activation of potassium/chloride ion flux
- 1:1 brain-to-plasma ratio in animal models demonstrates activity in CNS
- Safely dosed humans in Phase 1 healthy volunteer study

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KCC2 activators exhibit broad pharmacodynamic activity consistent with GABAergic inhibition

Model	Relevance	Rescue activity
Psychoses (Positive, negative & cognitive symptoms)		
MK801 induced hyperlocomotion (chronic, repeat dosing)	Psychosis, positive symptoms	✓
MK801 induced hyperlocomotion (single dose)	Psychosis, positive symptoms	✓
Amphetamine-induced hyper-locomotion model	Psychosis positive symptoms	✓
Methamphetamine induced psychosis	Psychosis positive symptoms | Cognition	✓
22Q deletion model (schizophrenia)	Cognition (working memory & task switching)	✓
Phencyclidine social interaction model	Negative symptoms - Sociability & physiological interactions	✓
Resident intruder model	Negative symptoms Reduced social withdrawal & aggression	✓
Huntington's disease motor symptoms (R6/2)	Motor function deficits	✓
Anxiety, stress & behavior		
Rett syndrome (MecP2-KO)	Rescue of behavior, sociability and subclinical seizures	✓
Chronic unpredictable stress	Lack of stress-induced weight loss	✓
Elevated plus maze	Anxiolytic properties	✓
SmartCube (phenotypic screen)	Wide range of attributes, including anxiolytic	✓
Chronic pain		
Paclitaxel induced pain	Neuropathic pain (Grip strength)	✓
Paw withdrawal threshold	Sensitivity to pain stimuli	✓
Epilepsies & seizures		
Kainate diazepam resistant model	Cessation of status epilepticus	✓
iPTZ model	Anticonvulsant	✓
Soman model	Anticonvulsant	✓

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OV4071 clinical plan: Near-term clinical validation with potential for rapid indication expansion

ONGOING	STARTING SOON	2027	
Phase 1 in Healthy Volunteers	**Ketamine challenge***	**Schizophrenia Phase 2 PoC**	**Phase 2 PDP & LBDP**
Laboratory and clinical safety, tolerability and PK Exploratory electrophysiology including qEEG and BOLD Elderly cohort	Exploratory electrophysiology: qEEG, ASSR, MMN, AAO, PPI Behavioral and clinical response Indication-relevant signal in an NMDA-antagonist model	Randomized, double-blind, placebo-controlled in acute schizophrenia PANSS change from baseline, CGI-S, Marder score, % responders Multi-site study in the U.S.	Single-arm, open label with titration up to two doses SAPS-H+D, electrophysiology, psychosis diary, PK/PD responders Multi-site study in the U.S.
DELIVERS **Dose selection and the human biomarker baseline**	DELIVERS **Human pharmacodynamic signal relevant to psychosis**	DELIVERS **Efficacy signal and effect size in acute schizophrenia**	DELIVERS **Signal and safety in neurodegenerative psychosis**

Electrophysiology biomarker strategy to predict potential clinical effects & inform indication selection

*Ketamine challenge to initiate pending PK characterization in the Phase 1 study. Development paths are not mutually exclusive and are dependent on global regulatory feedback.

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KCC2 activation is fundamental to schizophrenia neurobiology

Post-mortem analysis

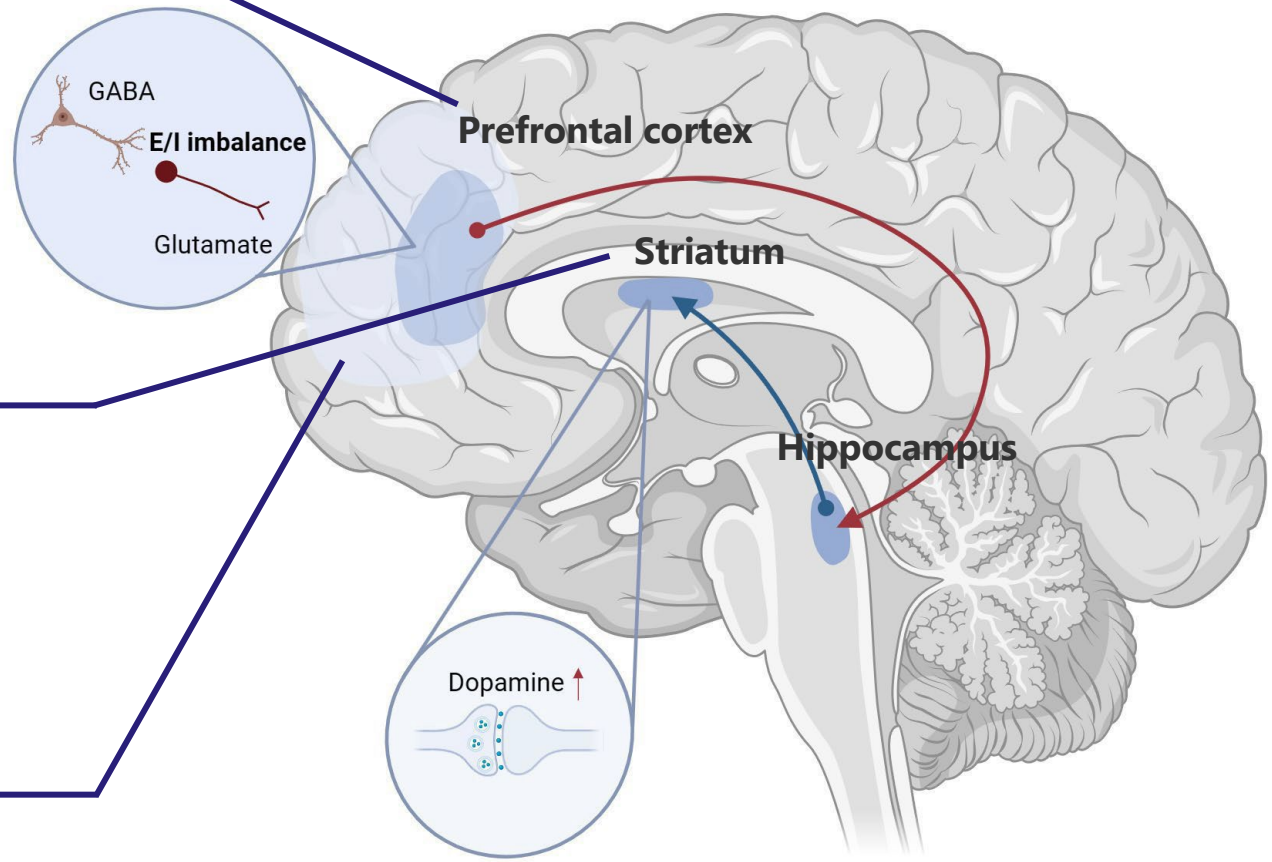
KCC2 expression reduced in the prefrontal cortex of human & animals with schizophrenia

Negative symptoms & cognition

KCC2 function in prefrontal cortex mediates brain circuits regulating negative symptoms and cognition

Positive symptoms

Glutamatergic-driven excitation in the prefrontal cortex drives excess dopamine in mesolimbic pathways and striatum, leading to positive psychosis and cognitive symptoms



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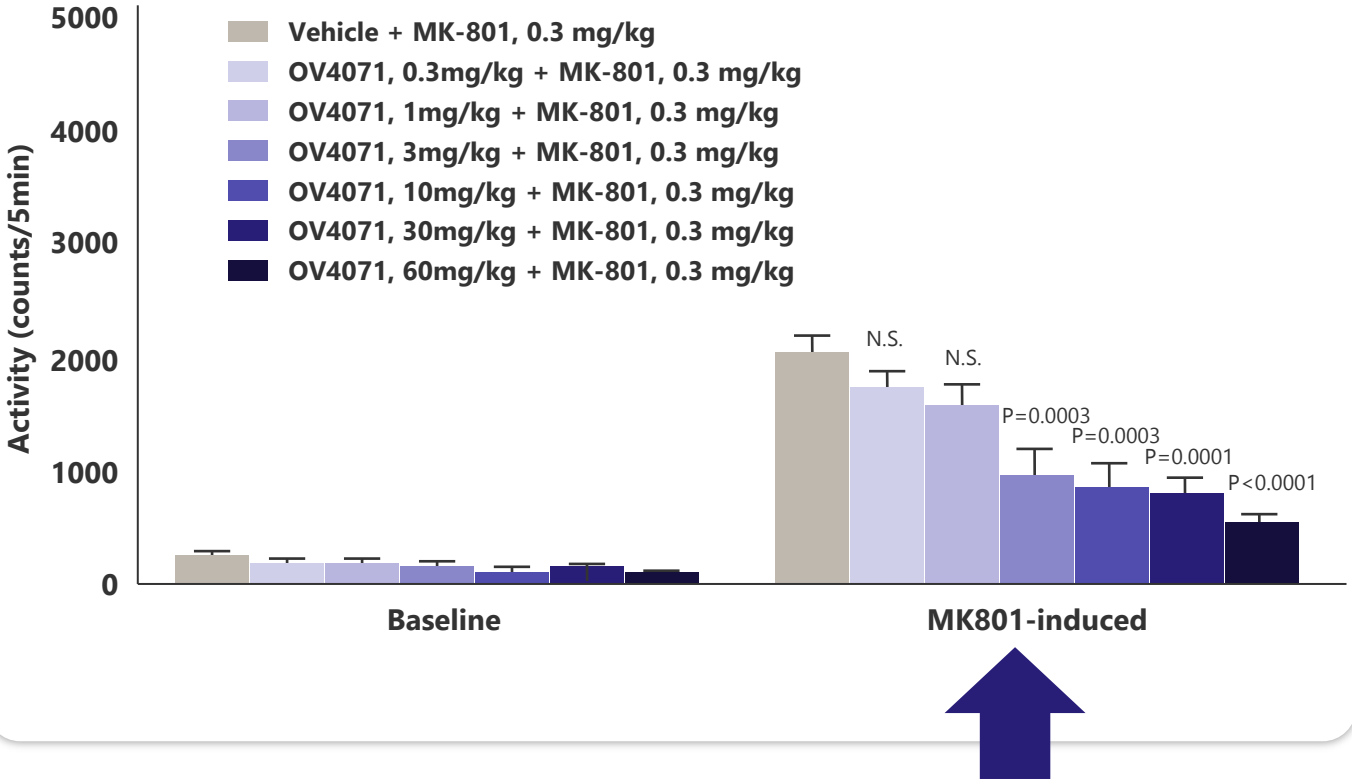
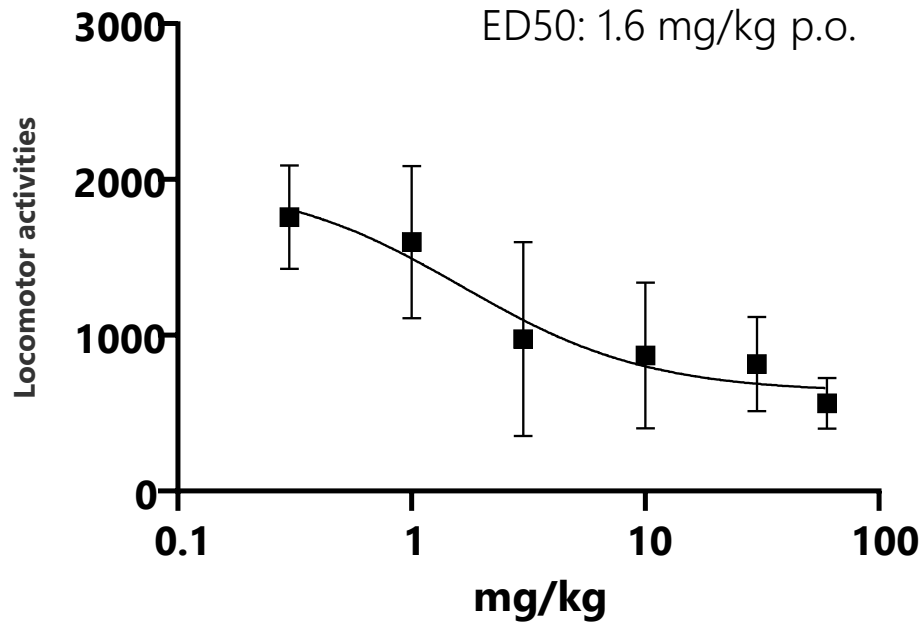
OV4071 delivers robust, dose-dependent signal in MK801 schizophrenia model

MK801 (NMDA antagonist) hyperlocomotion model comparing effect of vehicle to escalating doses of OV4071





OV4071 returned locomotion to natural levels (1,500 – 2,000 counts) in a dose-dependent fashion and reduced striatal dopamine

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OV4071 reduced levels of striatal dopamine in MK801 model

MK-801 (an NMDA antagonist that increases striatal dopamine)

- Increases extracellular concentration and firing rate of dopamine neurons

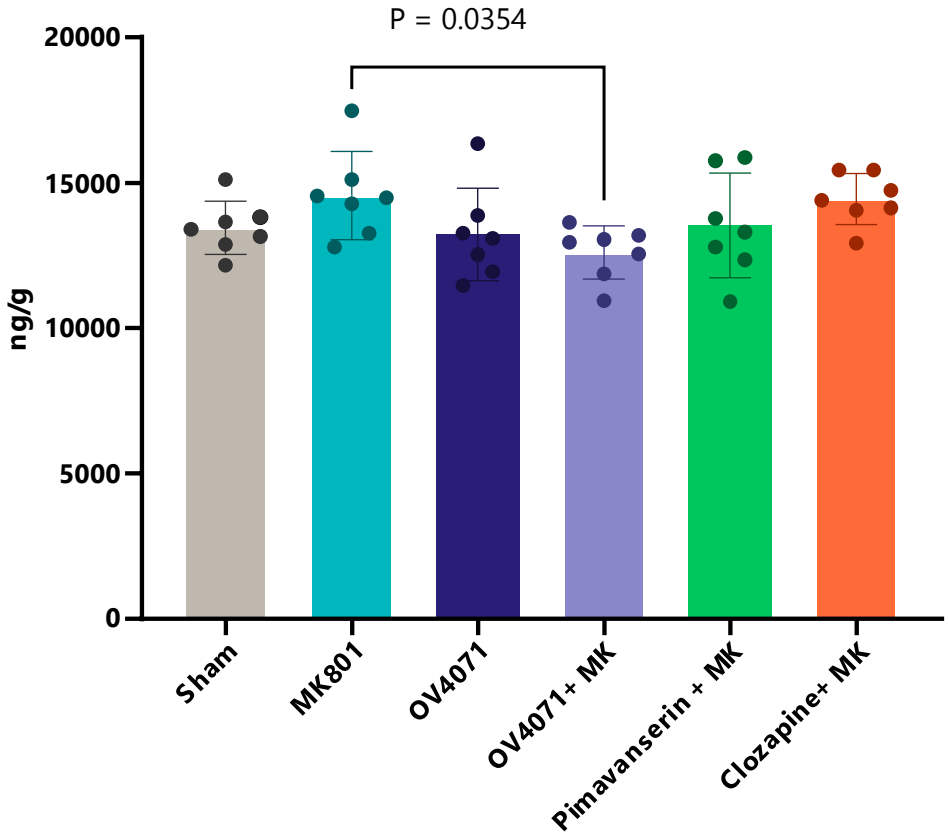
OV4071 decreased striatal dopamine levels

Results similar to pimavanserin and clozapine, which have a different mechanism of action

Results suggest

- A novel MOA for antipsychotic activities by KCC2 activation

Modulation of dopaminergic turnover in the striatum due to enhancement of GABAergic activity



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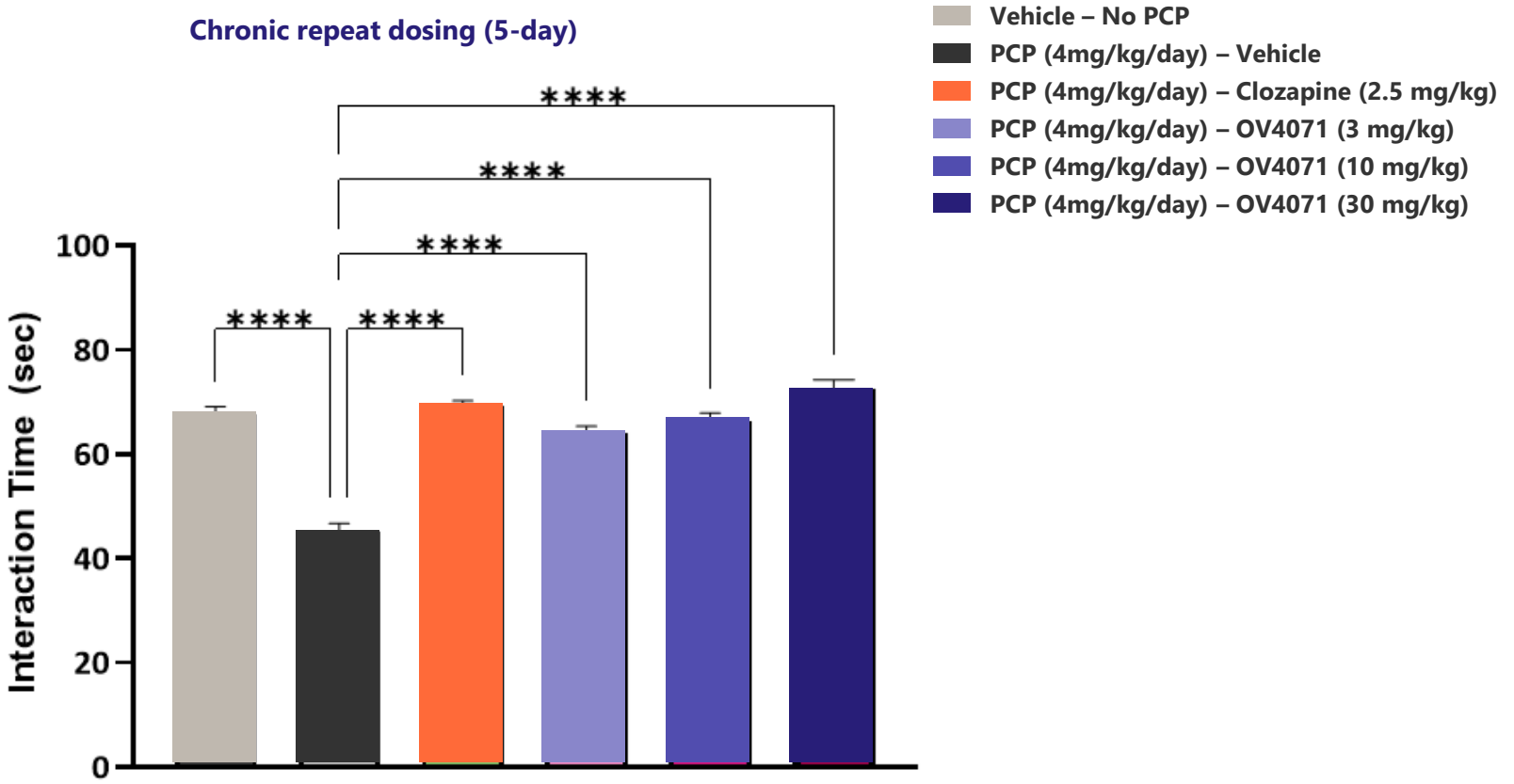
OV4071 restores social interaction in chronic PCP-induced animal behavior model (proxy for negative symptoms)

Methods

Induce asociality and reduced interactions with phencyclidine

Results

- OV4071 restored typical animal physiological interactions consistent with:
  - Natural control
  - Clozapine
- E/I is restored, suggesting a complementary mechanism of action



*Effects of clozapine and OV4071 on interaction time in rats chronically treated with PCP. Data are presented as mean ± SEM. ***p<0.0001 compared to PCP-Vehicle group.*

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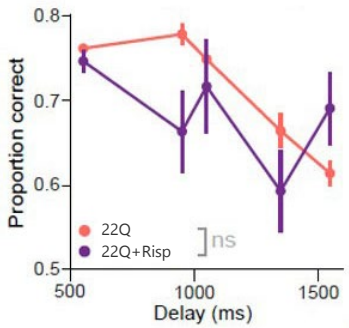
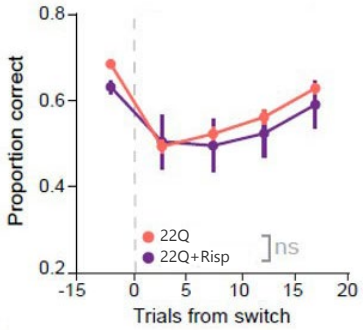
KCC2 direct activation vs. marketed antipsychotics in a genetic model (22q11 deletion) of psychotic disorders including schizophrenia

Antipsychotics (risperidone)

Working memory

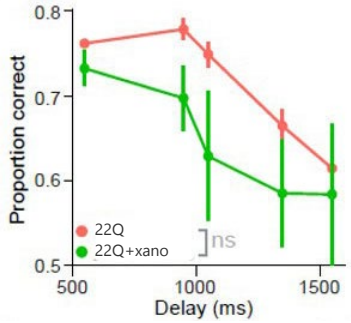


Task switching

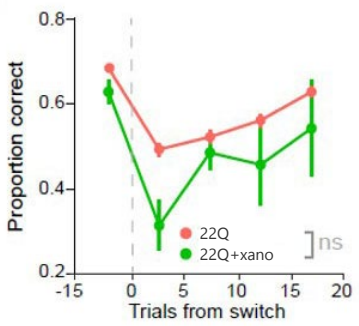


Xanomeline/trospium (Cobenfy)

Working memory

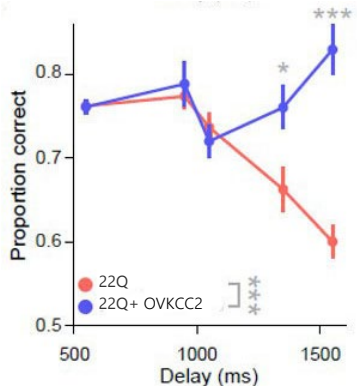


Task switching

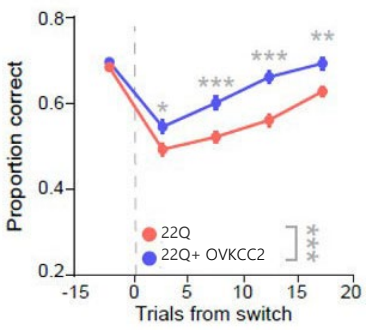


Ovid KCC2 direct activator

Working memory



Task switching



Ovid KCC2 direct activator provides benefits across working memory and task switching in 22q11 deletion mice

Data source: Mukherjee et al., in preparation

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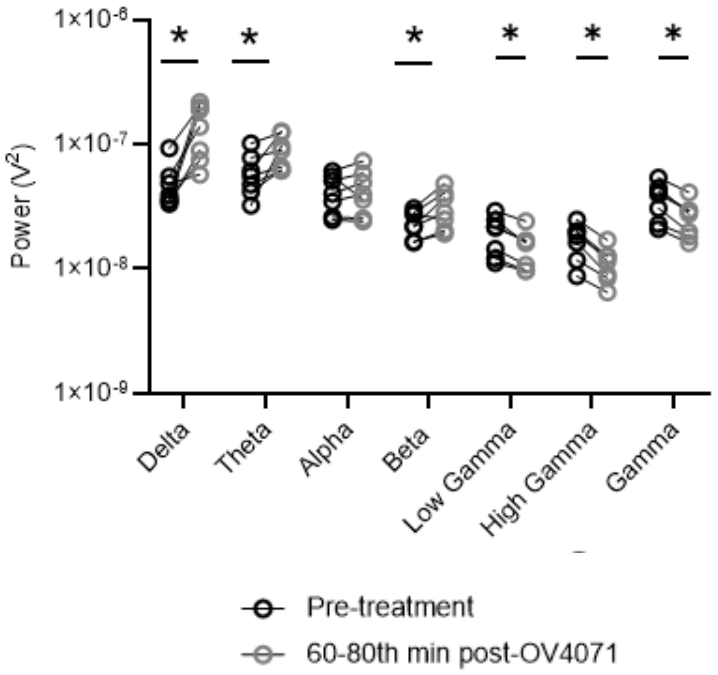
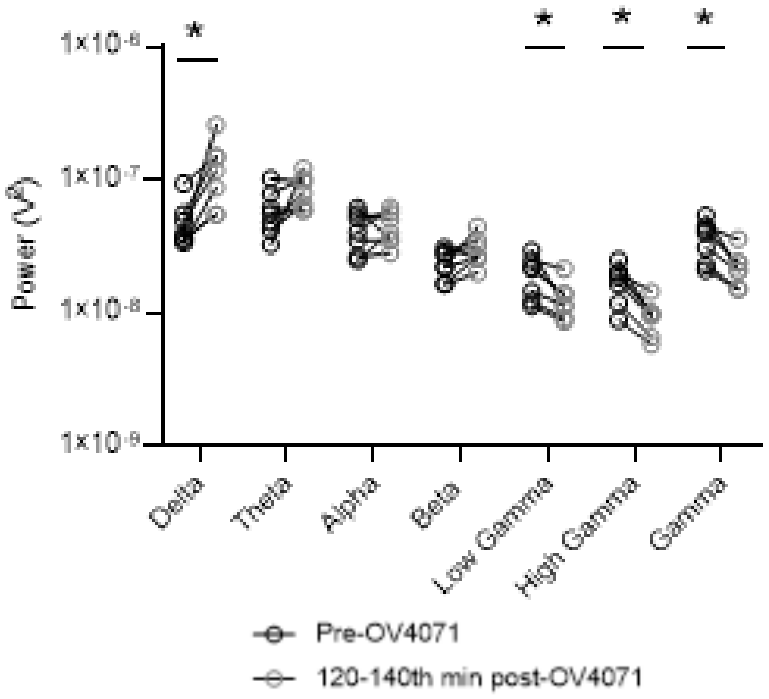
OV4071 demonstrates potentially translatable EEG biomarkers

Wild type mice
(OV4071 3.75 mg/kg)

60 – 80 mins post dose

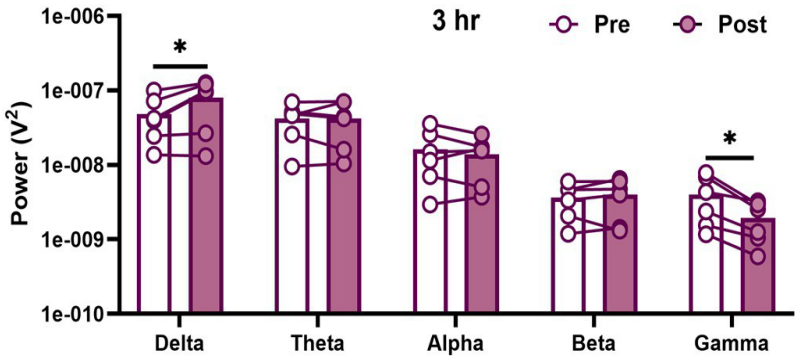


120 – 140 mins post dose



MECP2 (Rett) mice
(OV4071 7.5 mg/kg)

3 hours post dose



N= 6 animals; pairwise t-test, *p<0.05

Biomarkers establish GABAergic activity in multiple animal models

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A meaningful psychosis market for OV4071

~1.8M addressable US+EU5 patients with treatment-resistant schizophrenia in 2038

~700K ED visits a year, with **~400K** hospitalizations

Existing treatments have limited efficacy, significant side effects, and fail to address underlying brain circuit dysfunction

One therapy approved for PDP only with poor efficacy and significant safety concerns

~770K addressable US+EU5 patients in 2038

~40% of PD[2] and **~61%** of LBD patients experience psychosis

OV4071 branded market share, market access & compliance ≈278K pts on therapy (102K PD-P+DLB-P, 176K SCZ)

Premium pricing $36K US, $21.5K EU

~$6.8 Billion Peak US[1] + EU5 Revenue in 2038

1. Estimates for peak OV4071 revenue in 2038; LifeSci Consulting
2. Mayeli et al. 2022

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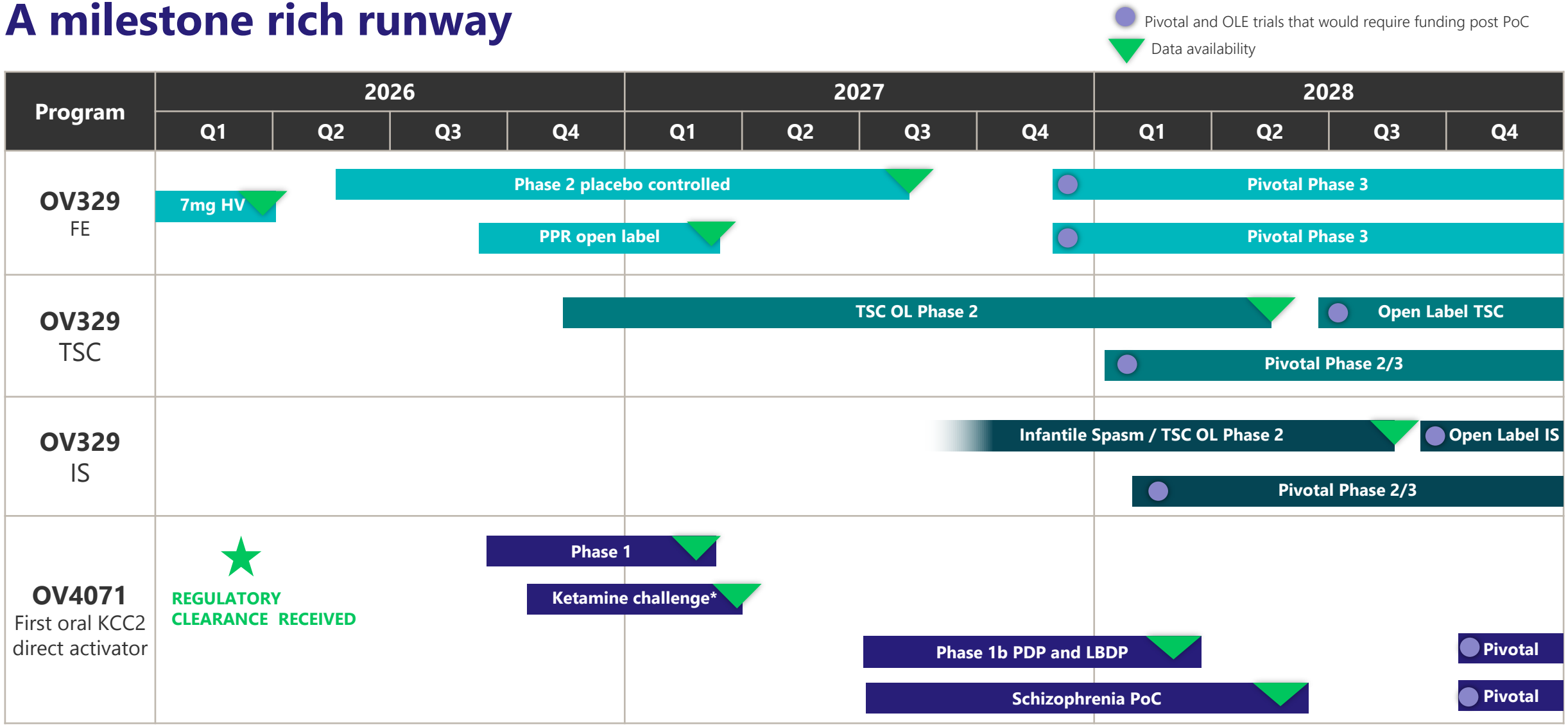
A milestone rich runway



Timelines pending feedback from regulatory discussions
*Ketamine challenge to initiate pending PK characterization in Phase 1 study
**Assumes exercise of all current outstanding warrants

Cash runway into 2029 fueling multiple catalysts**

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