

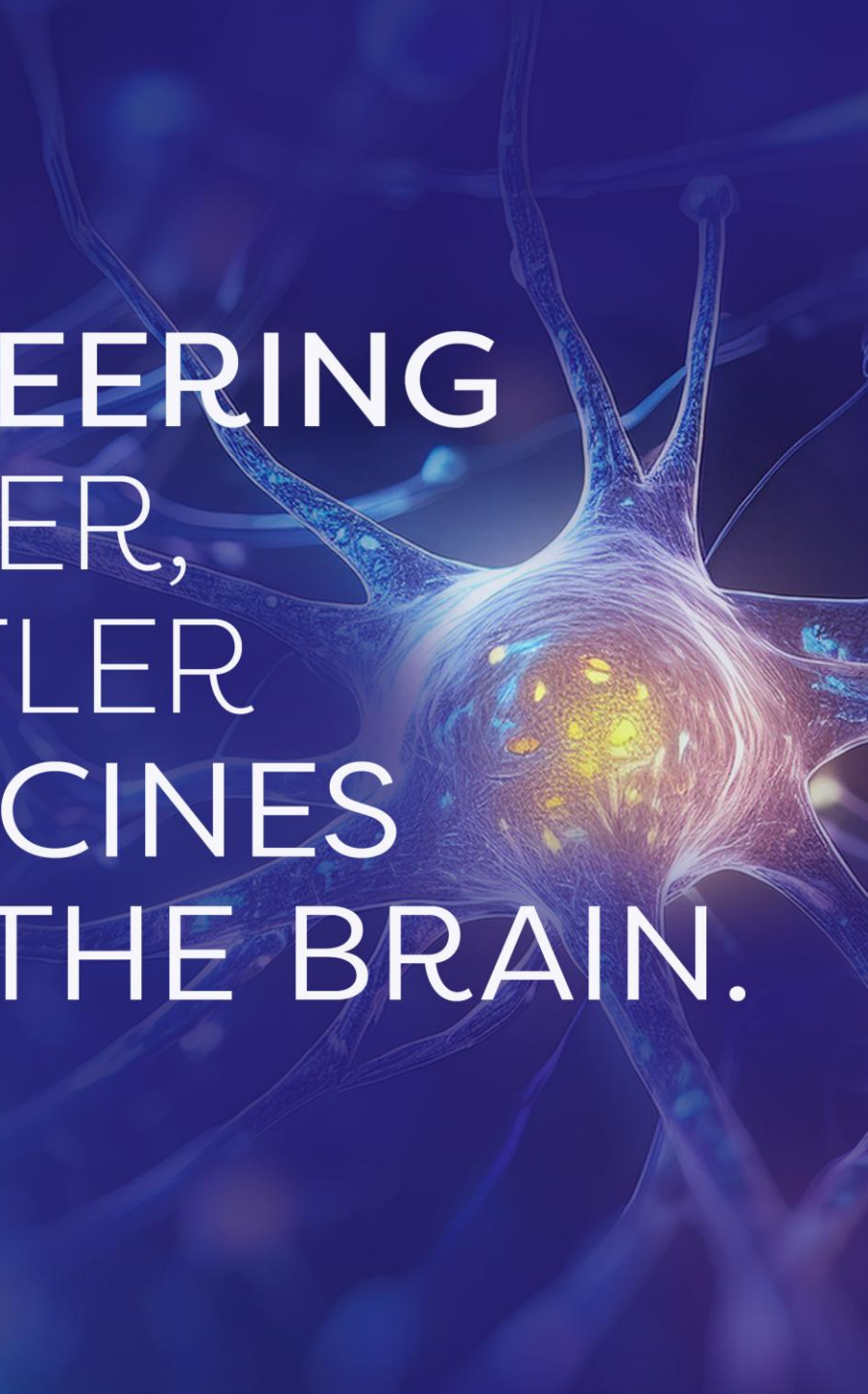


Welcome

KCC2

Deep Dive Day

April 14, 2026

A detailed illustration of a neuron, showing its cell body (soma) with a bright yellow and orange nucleus, and several branching dendrites and an axon extending outwards. The background is a deep blue with faint, glowing neural pathways.

PIONEERING
BETTER,
GENTLER
MEDICINES
FOR THE BRAIN.



OVID strategy & the KCC2 opportunity

Meg Alexander, President & Chief Executive Officer

Ovid Therapeutics

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; 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).

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 fact nor 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, and the risk that Ovid may not be able to realize the intended benefits of its business strategy. 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 most recently filed Annual Report on Form 10-K and Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission (“SEC”), and in subsequent and 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.

Our vision

Pioneering a new class of medicines for a “master switch” in the CNS

Potential “pipeline in a product” of better, gentler medicines

Efficient path to proof-of-concept

OV4071 is an oral KCC2 activator well suited for drug development

Opportunity to address major unmet needs in large and growing indications

Our speakers & agenda



Focus: medicines to quell conditions caused by neural hyperexcitability

Fundamental biological targets

implicated in many conditions driven by neural hyperexcitability

Differentiated, universal mechanisms of action

that may hold broad therapeutic utility and stand out in a growing field of me-too medicines

Pipeline of highly specific small molecules

intended to culminate in a fully-integrated neurotherapeutics company

Multiple anticipated clinical & regulatory milestones throughout 2026 - 2027

High-value, differentiated pipeline

Programs	Potential Opportunity	Preclinical	Phase 1	Phase 2	Anticipated milestones*
OV329, a next-generation GABA-aminotransferase inhibitor					
Drug-resistant adult focal onset seizures (FOS)	Novel mechanism of action in FOS with: - Competitive efficacy - Superior tolerability & safety - No expected titration or drug:drug interactions	Phase 2 RCT			- Phase 2 initiation (Q2 2026) - Open-label photo paroxysmal response (PPR) initiation and results H2 2026 - Phase 2a topline results (mid-2027)
		Open label photo paroxysmal response PoC			
Tuberous sclerosis complex seizures (TSC)	1 st approved GABA-AT inhibitor - Preferable safety, tolerability - Increased treatment duration	PoC & safety			PoC safety and signal finding study to initiate in Q4 2026
Infantile spasms (IS)	Disease modifying 1 st line agent - Preferable safety, tolerability - Increased treatment duration	PoC & safety			Infant formulation and enabling studies ongoing
OV4071, potassium-chloride cotransporter 2 (KCC2) direct activator (oral)					
Broad spectrum psychosis	- Psychosis associated with Parkinson's disease and Lewy body dementia - Acute schizophrenia Additional indications: - Neurodegenerative psychoses - Other undisclosed indications	Phase 1			- Phase 1 initiation (Q2 2026) - Proof-of-mechanism ketamine study (initiation H2 2026) - Phase 1b PoC studies & results (H2 2026 - 2027)
		Ketamine study			

Additional undisclosed KCC2 development candidates from unique direct activator portfolio

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

High-value, differentiated pipeline

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Unique mechanisms of action in areas of great unmet need

Focal onset seizures

Multiple potassium,
sodium, SV2a programs.



**No safe approved
GABA-AT inhibitors**

Tuberous sclerosis complex



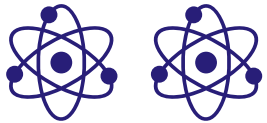
2 approved drugs in the
last **10 years**

Infantile spasms



0 new medicines
in the last **20 years**

Schizophrenia



2 new mechanisms
in **20 years**

Parkinson's disease psychosis



1 medicine
approved

Lewy body dementia

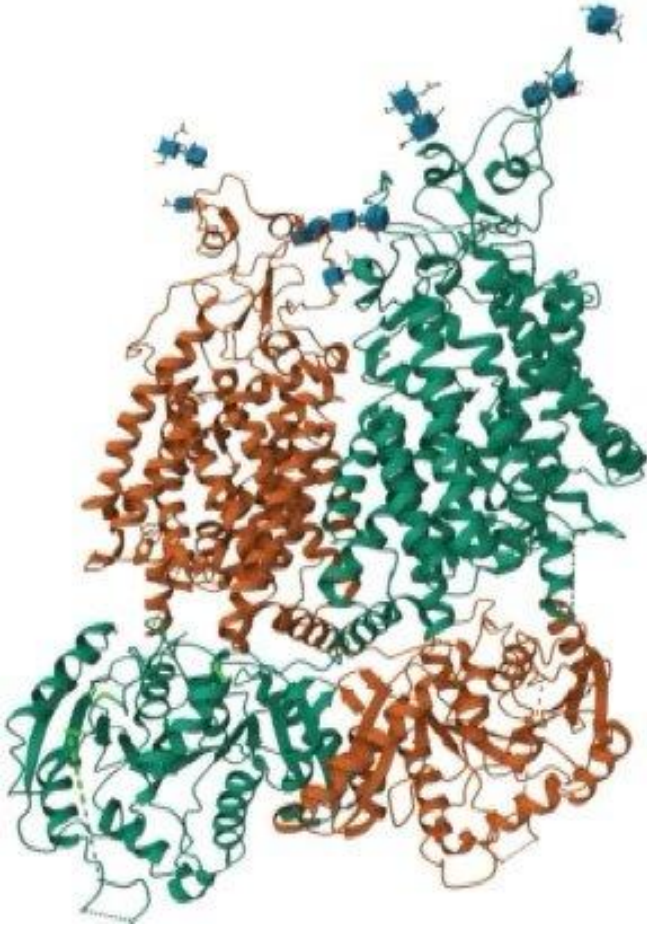


0 medicines

THE KCC2 OPPORTUNITY

ONE : **MANY**
mechanism medicines

KCC2: a common “master switch” regulating neural excitatory/inhibitory balance



Exclusively expressed in the CNS

Precision mechanism of action to rebalance neural network hyperexcitability

Restores neural sensitivity to GABA and thereby regulates synaptic inhibition

- Upstream of neurotransmitter blockers (e.g., D2 antagonists)
- Downstream of many acquired and genetic causes of hyperexcitability

Function occurs only when the transporter is suboptimally extruding chloride

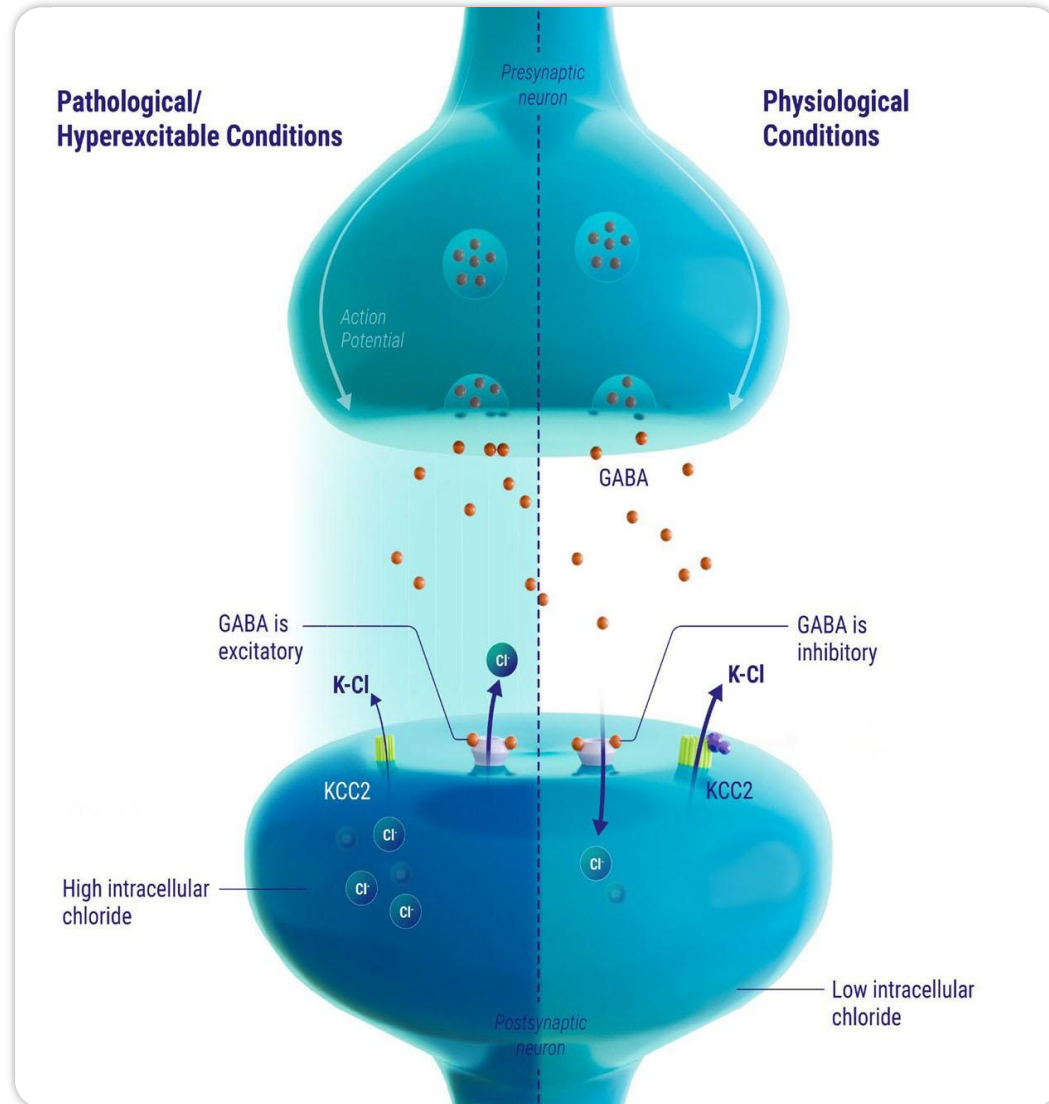
Converges on a broad spectrum of disorders with hyperexcitability

Self-limiting chemical gradient makes it nearly impossible to overmodulate

KCC2 direct activation: Mechanism of action

Impaired KCC2 activity

- Causes high intra-neuronal chloride concentrations
- Leads to abnormal depolarizing of the GABA receptor
- Causes neuronal hyperexcitability



Normal KCC2 activity

- KCC2 activity is high
- Leads to low intra-neuronal Cl⁻ concentration
- Enables a GABA-driven influx of Cl⁻, causing an inhibitory effect (hyperpolarizing) to the GABA_A current

KCC2 direct activation improves chloride extrusion and thereby, GABAergic inhibition

Therapeutic opportunity: KCC2 direct activation

Neurodegenerative psychoses & cognition

- Schizophrenia
- Alzheimer's agitation
- Alzheimer's hallucinations & delusions
- Parkinson's disease psychosis
- Lewy body dementia
- Huntington's disease delusions
- Bipolar mania

Conditions of anxiety & behavioral dysregulation

- Generalized anxiety disorder
- Obsessive compulsive disorder

Neurodevelopmental conditions

- Rett syndrome
- Developmental and epileptic encephalopathies
- Autism spectrum disorders

Pain & trauma

- Neuropathic pain
- Centralized pain
- Audiogenic trauma
- Spinal cord injury

One mechanism: MANY medicines

Robust armamentarium of pharmacodynamic evidence

**Findings
reinforce
restoration of
E/I balance**

**Consistent
with KCC2
mechanism
of action**

Ovid KCC2 direct activators

Model	Relevance	Rescue Activity
Psychosis & locomotion		
MK801 induced hyperlocomotion (repeat dose)	Psychosis, schizophrenia	✓
MK801 induced hyperlocomotion	Psychosis, schizophrenia	✓
Methamphetamine induced psychosis	Psychosis & cognition	✓
22Q deletion model (schizophrenia)	Schizophrenia	✓
Huntington's disease motor symptoms (R6/2)	Motor function deficits	✓
Amphetamine model	Psychosis	✓
PCP social interaction model	Sociability & physiological interactions	✓
Anxiety & behavior		
Rett syndrome (MecP2-KO)	Behavior; sociability	✓
Elevated plus maze	Agitation vs. anxiolytic properties	✓
SmartCube (phenotypic screen)	Wide range of attributes	✓
Pain		
Paclitaxel induced pain	Neuropathic pain (Grip strength)	✓
Paw withdrawal threshold	Sensitivity to pain stimuli	✓
Epilepsies & seizures		
Kainate diazepam resistant model ¹	Cessation of status epilepticus	✓
iPTZ model	Anticonvulsant	✓
Soman model ¹	Anticonvulsant	✓



The KCC2 opportunity: Restoring excitatory/inhibitory balance in the brain

Oliver Howes, MD, PhD

Kings College & Imperial College London

Schizophrenia: neurobiology

Glutamate-driven excitation in the prefrontal cortex surges striatal dopamine, leading to positive psychosis and cognitive symptoms

Genetics & epigenetics

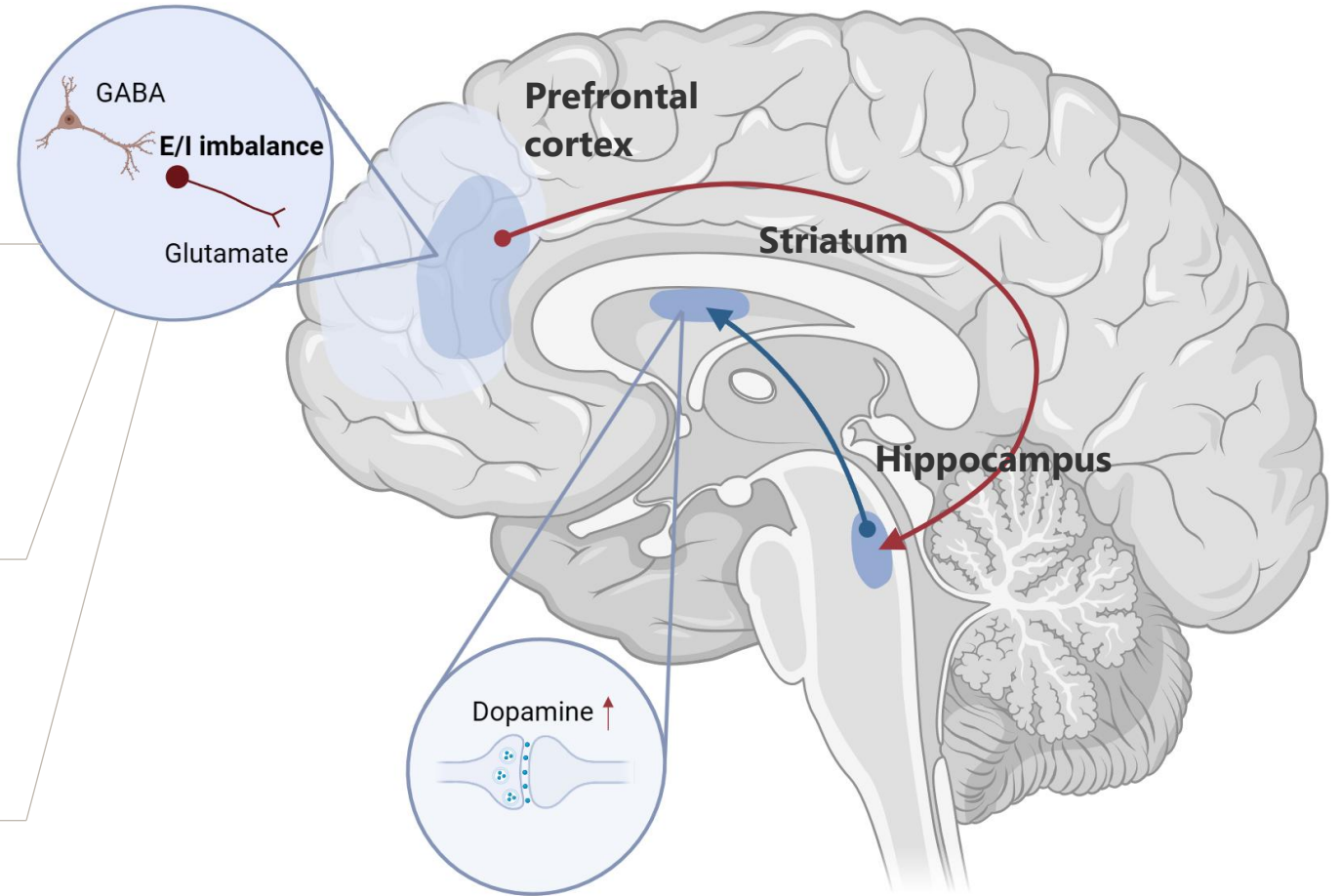
Excitatory pathways

Post-mortem

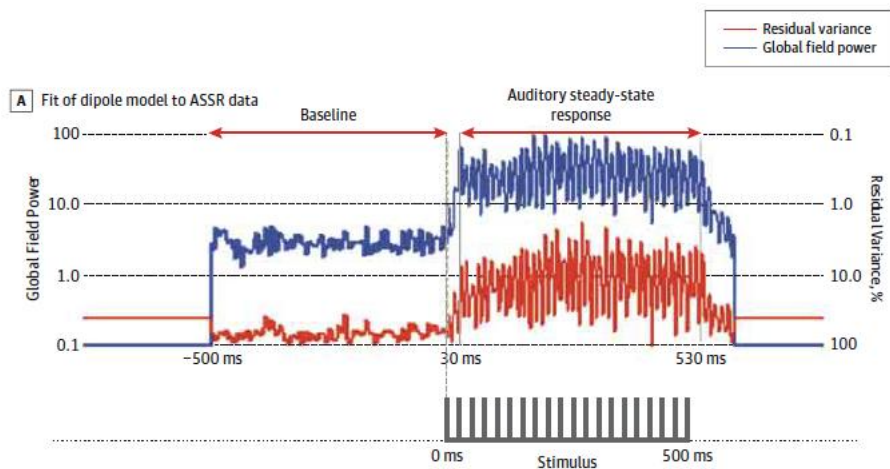
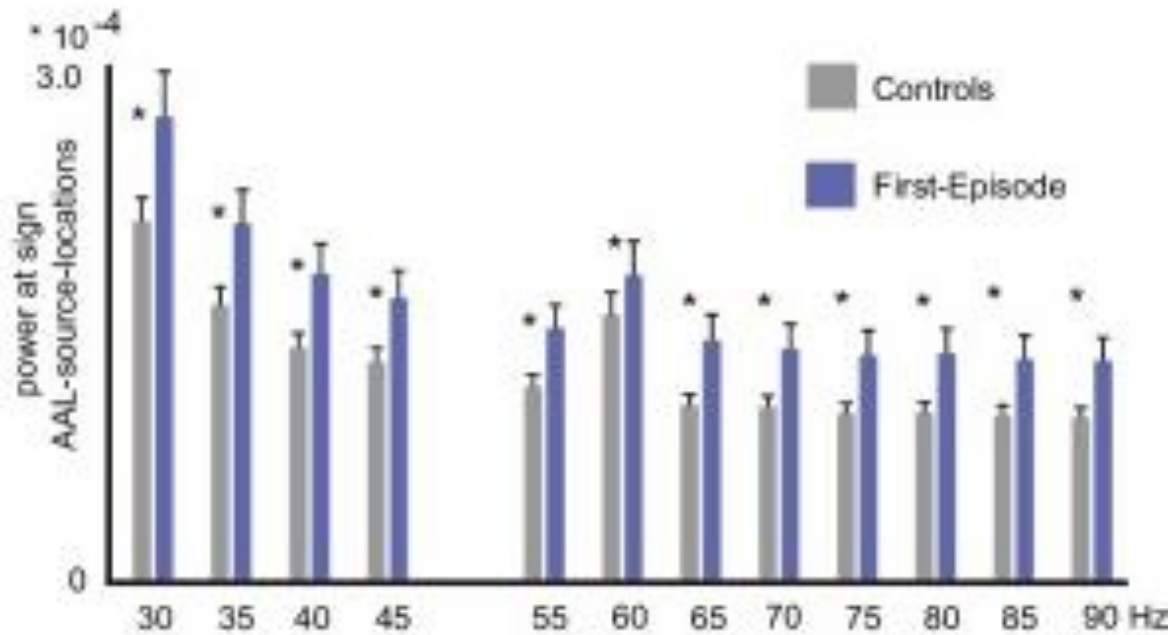
Confirmed loss of inhibitory markers

Imaging

Altered activity: EEG, fMRI, PET



Schizophrenia: higher cortical high-frequency activity

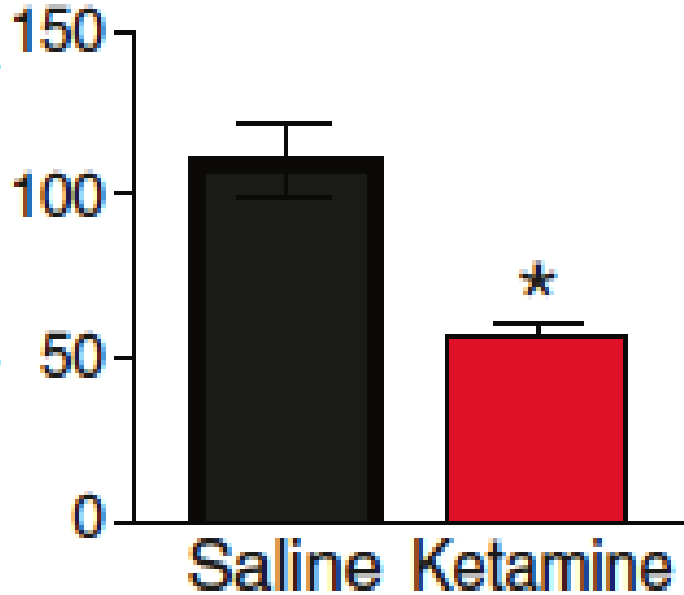


Hirano et al 2015; Grentt-Jong et al 2018

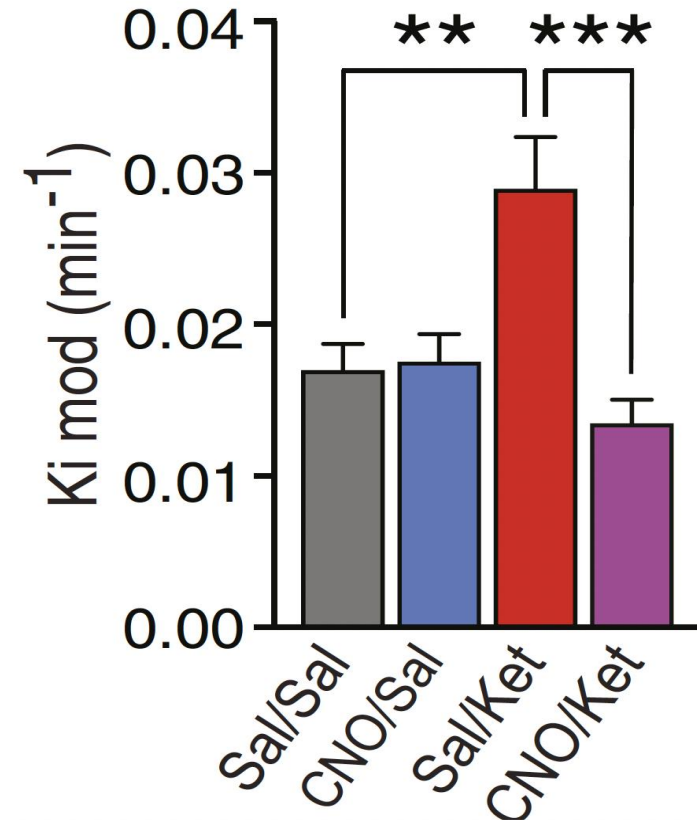
Loss of cortical inhibition drives striatal dopamine overactivity

Inhibitory
marker

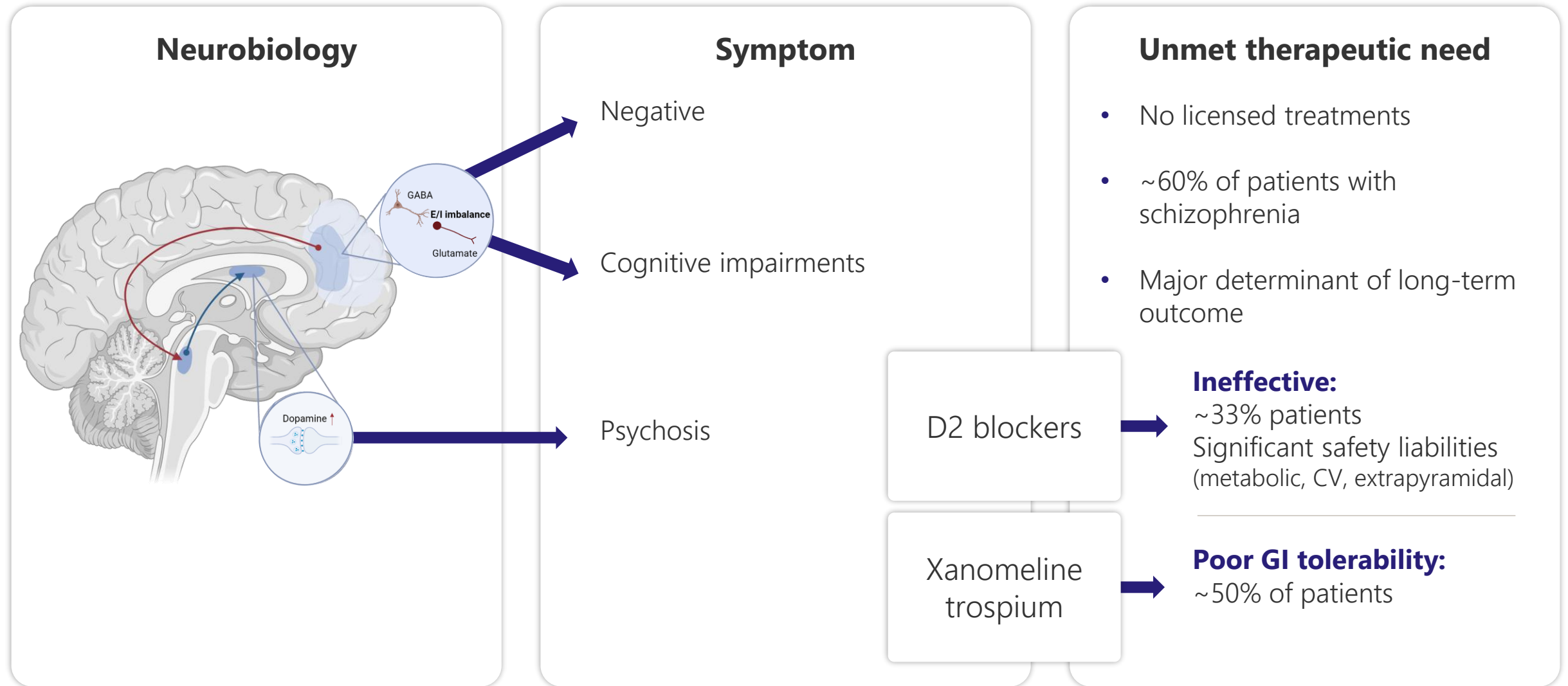
Median Fluorescence
/cell (% of saline)



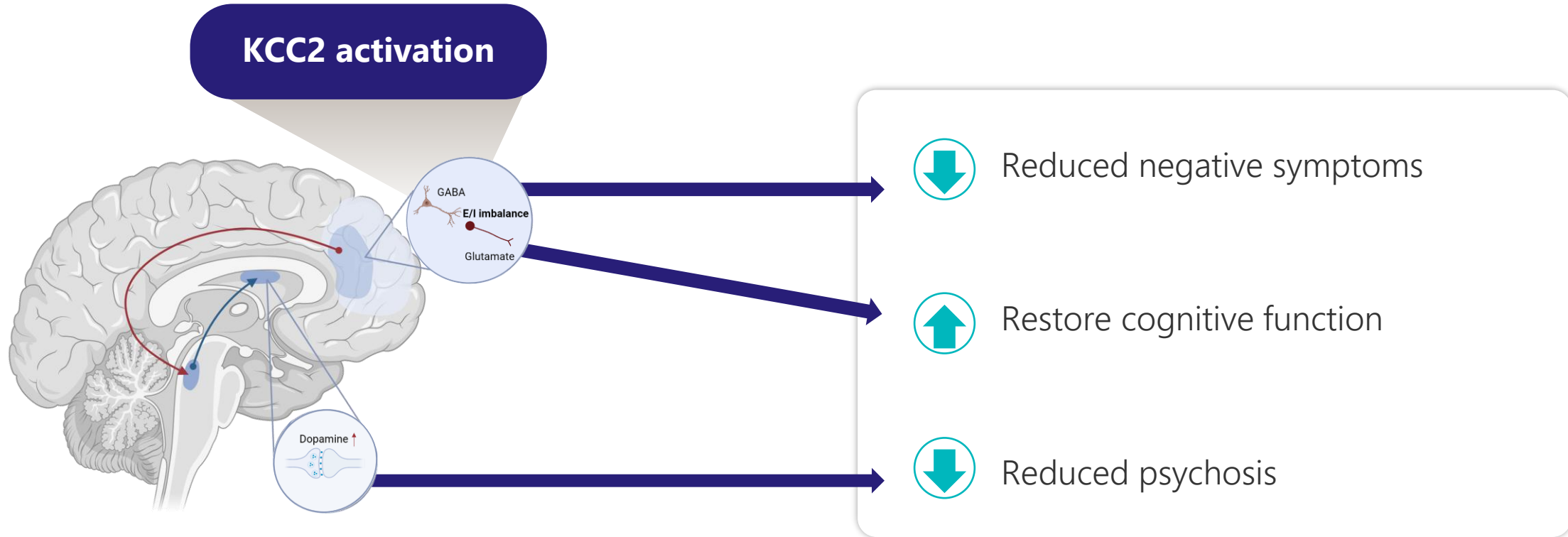
Dopamine
activity



Unmet need in schizophrenia



Schizophrenia: potential role of KCC2 activator



KCC2 activation enhances GABAergic inhibition with a restoration of E/I balance with multiple regional consequences

- Reduce psychosis due to a dopaminergic surge in the striatum
- Improve negative symptoms
- Rescue cognition through a preservation of dopaminergic function in the PFC

Parkinson's disease psychosis

Prevalence

~40% of patients will suffer from psychosis¹

PD and LBD patients with hallucinations have **decreased GABA in the visual cortex^{2,3}**

Cortical E/I imbalance

**Delusions:
~15%**

**Cognitive
impairment**

**Hallucinations:
~28%**



1. Mayeli et al. 2022
2. Firbank et al 2018
3. Khundakar et al 2016

Parkinson's disease psychosis

Few approved treatments:

Clozapine

- Not indicated for PDP
- Metabolic concerns

Dopaminergic/
serotonergic
blocker → 

Pimavanserin

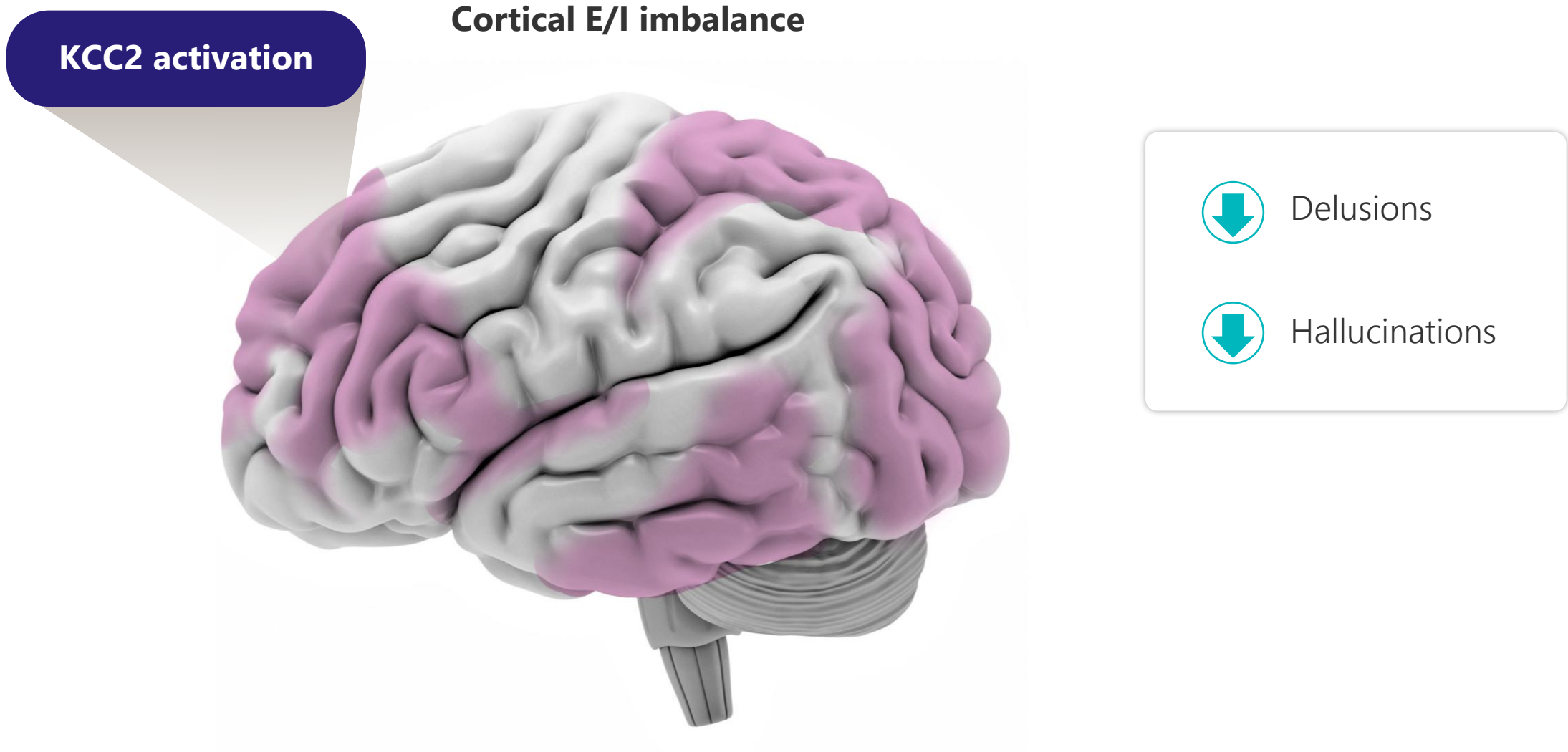
- Limited efficacy
- Limiting side effects

5HT2a partial
agonist → 

Cortical E/I imbalance



Parkinson's disease psychosis: potential role of KCC2 activator





Restoring function in psychotic disorders with KCC2 activation

Michael Halassa, MD, PhD

Virginia Tech

KCC2 expression is lower in the schizophrenia prefrontal cortex



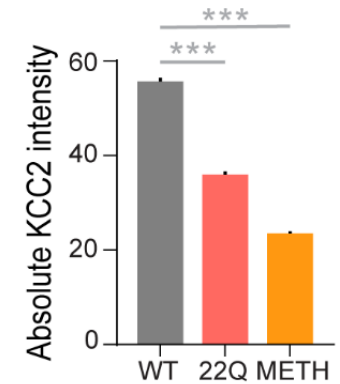
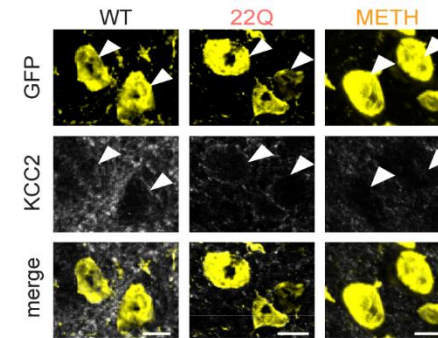
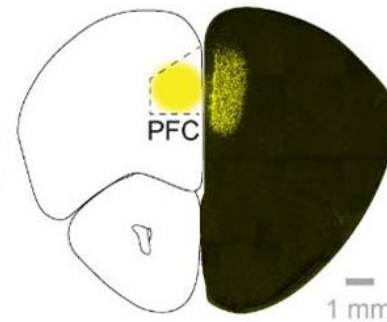
Decreased KCC2 expression in PFC of people with schizophrenia versus control subjects (postmortem brain samples)

KCC2 reduction also seen in multiple mouse models relevant to schizophrenia

Both animals exhibited a reduction in excitatory neuronal PFC KCC2 expression

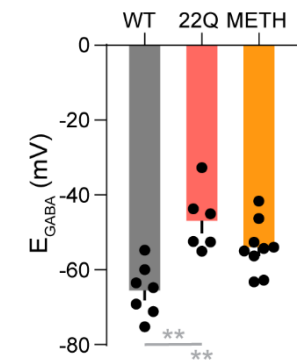
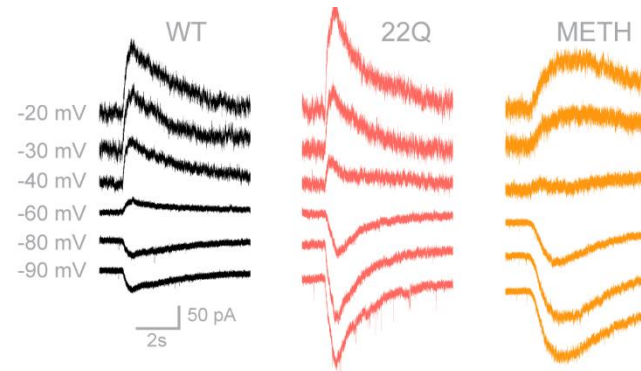
Other brain regions were normal, suggesting a unique specificity of KCC2 expression in the PFC

KCC2 expression in PFC across two models relevant to schizophrenia



PFC pyramidal neurons exhibited depolarized GABA reversal potential (E_{GABA})

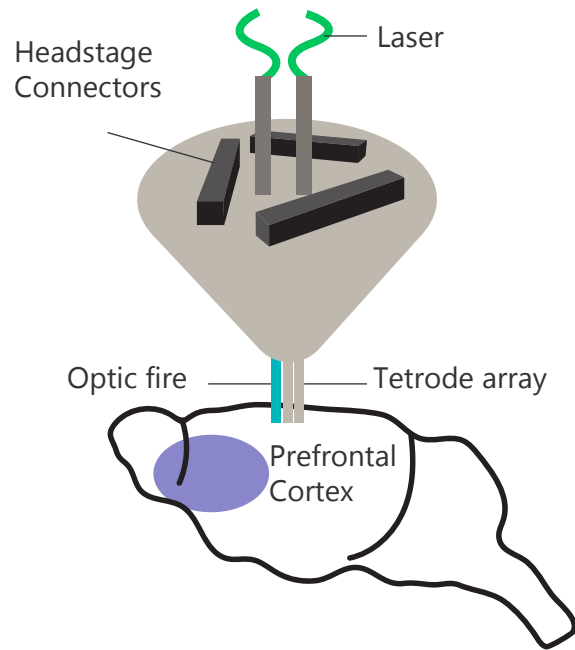
Both animals show less efficacious GABAergic signaling



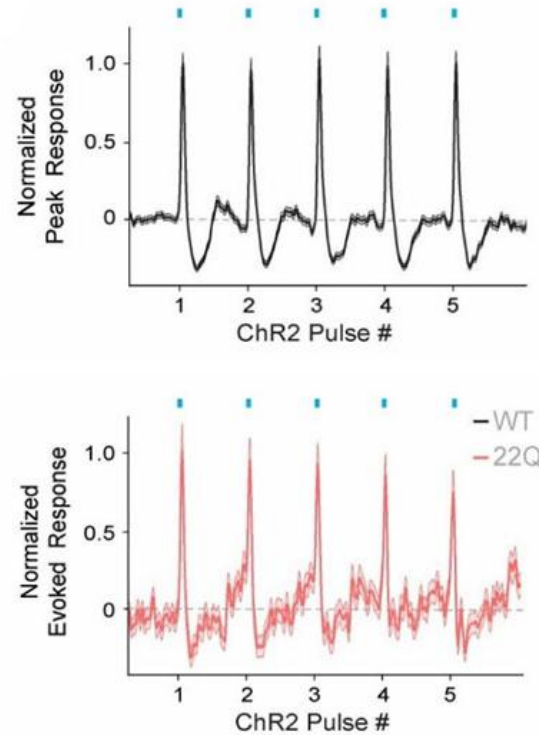
PFC KCC2 expression and function is diminished in two schizophrenia-relevant models

E/I balance and prefrontal signal processing is impaired in models relevant to schizophrenia (example shown: 22q11 deletion)

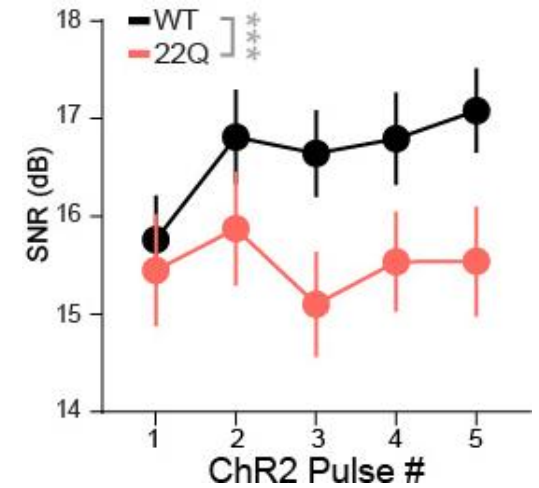
Engaging prefrontal signal processing with optogenetics



PFC E/I balance is perturbed in animals with 22q deletion



PFC signal processing is degraded in animals with 22q deletion



Behavioral impact of diminished KCC2 in schizophrenia-relevant models

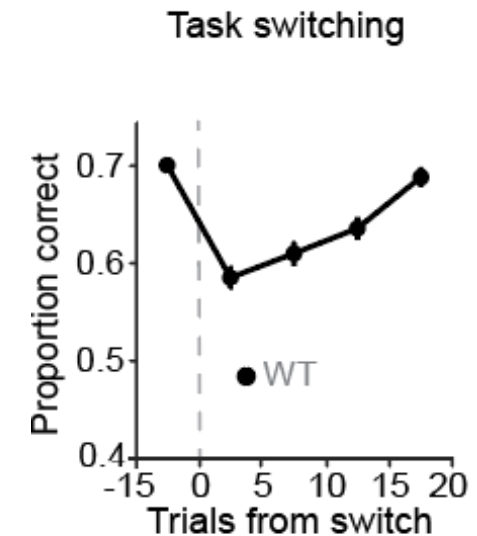
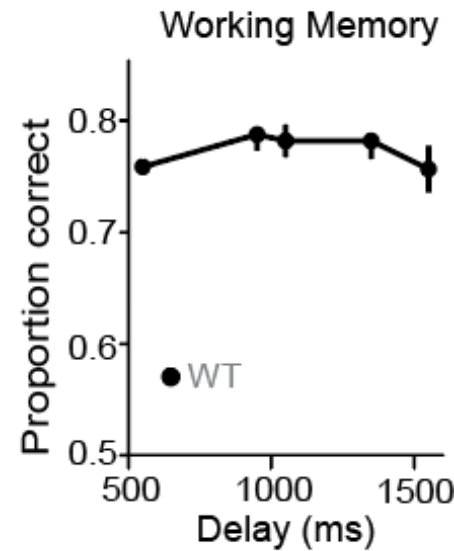
Objective

Evaluate PFC function in behavioral readouts

Utilize a validated cognitive task that includes working memory and task switching

Novel attention control task

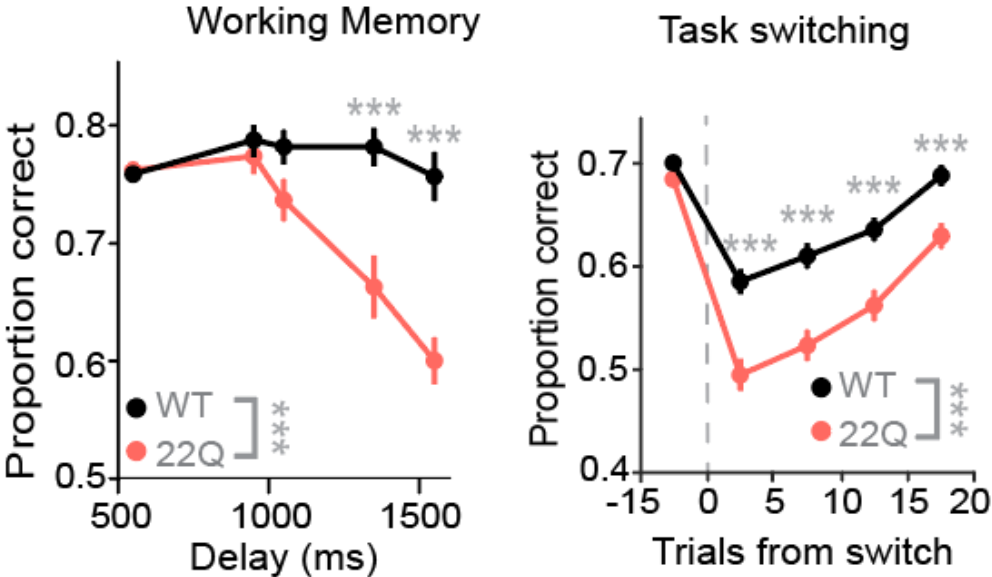
Established cognitive behavior of wild type mice



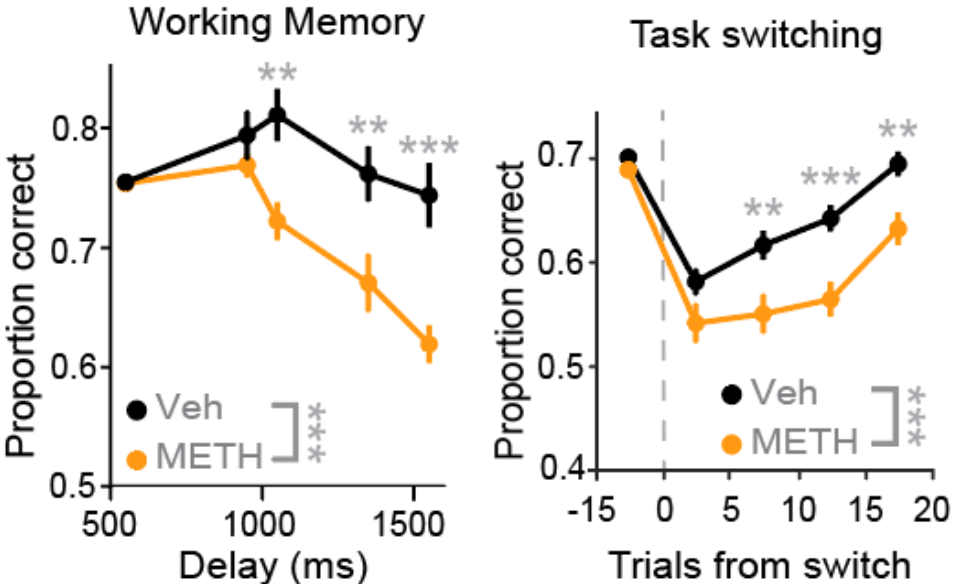
1. Wimmer et al., Nature, 2015
2. Schmitt et al., Nature, 2017
3. Rikhye et al., Nature Neuroscience, 2018
4. Nakajima et al., Neuron, 2019
5. Mukherjee et al., Nature, 2021
6. Zhou et al., Nature Neuroscience, 2026

Comparable cognitive deficits observed across schizophrenia-relevant models

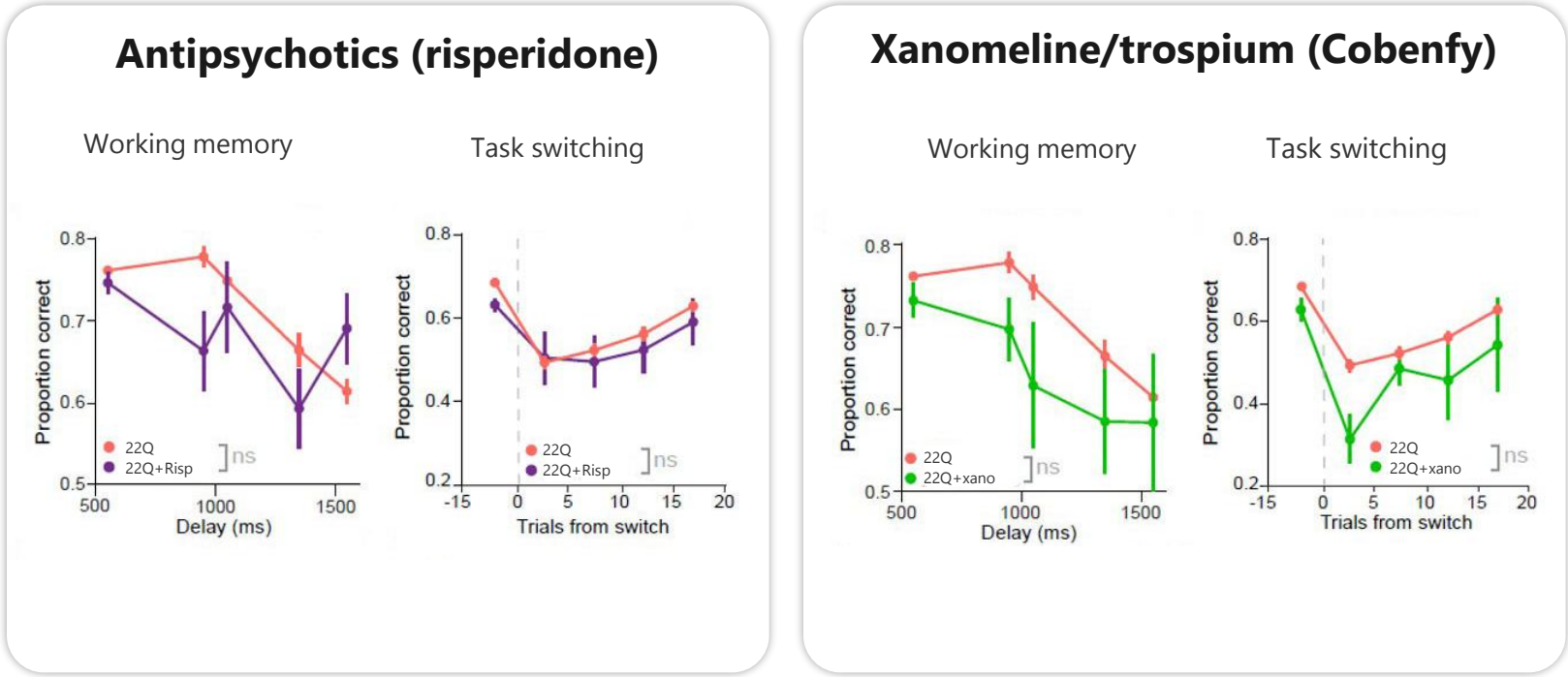
Impaired working memory & task switching in 22q11 deletion mouse



Impaired working memory & task switching in chronic methamphetamine model



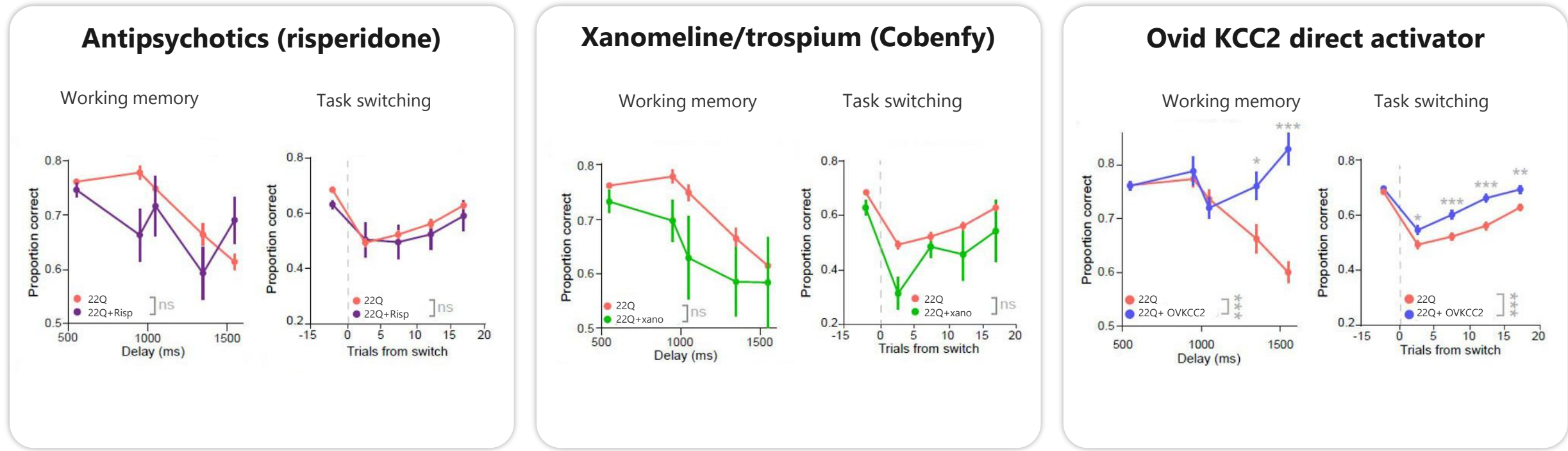
KCC2 direct activation vs. marketed antipsychotics in a genetic model of psychotic disorders



Ovid KCC2 direct activator provides benefits across both domains in 22q11 deletion mice

Data source: Mukherjee et al., in preparation

KCC2 direct activation vs. marketed antipsychotics in a genetic model of psychotic disorders



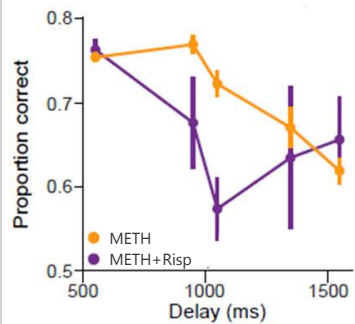
Ovid KCC2 direct activator provides benefits across both domains in 22q11 deletion mice

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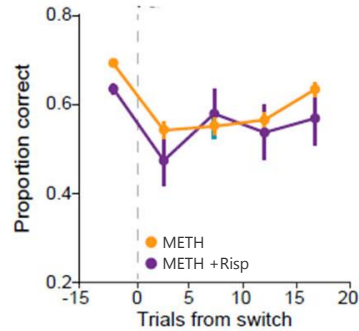
KCC2 direct activation vs. marketed antipsychotics in a pharmacological model of psychotic disorders

Antipsychotics (risperidone)

Working memory

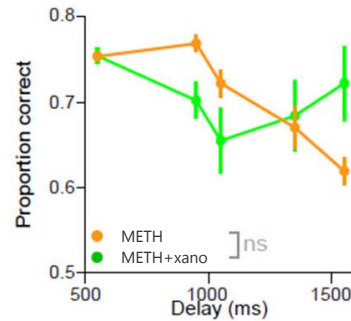


Task switching

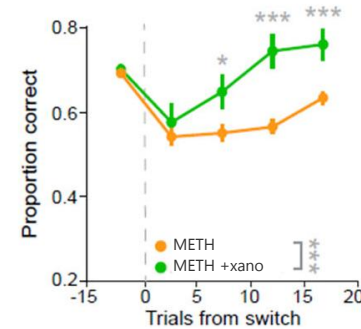


Xanomeline/trospium (Cobenfy)

Working memory



Task switching



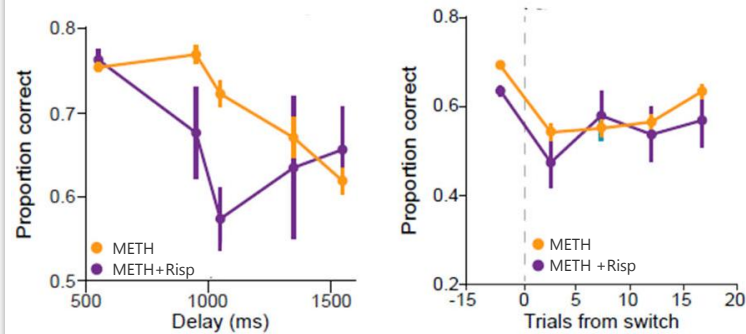
Ovid KCC2 direct activator outperformed in working memory relative to risperidone and xanomeline (Cobenfy active ingredient) and provided task switching benefit compared to risperidone

KCC2 direct activation vs. marketed antipsychotics in a pharmacological model of psychotic disorders

Antipsychotics (risperidone)

Working memory

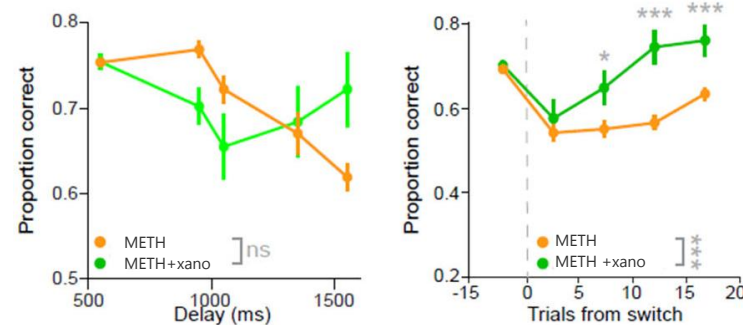
Task switching



Xanomeline/trospium (Cobenfy)

Working memory

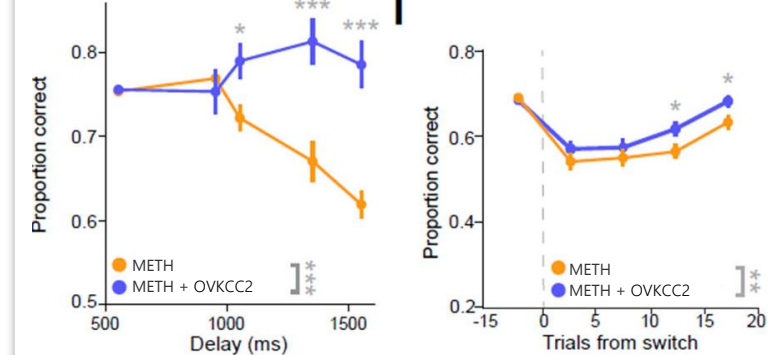
Task switching



Ovid KCC2 direct activator

Working memory

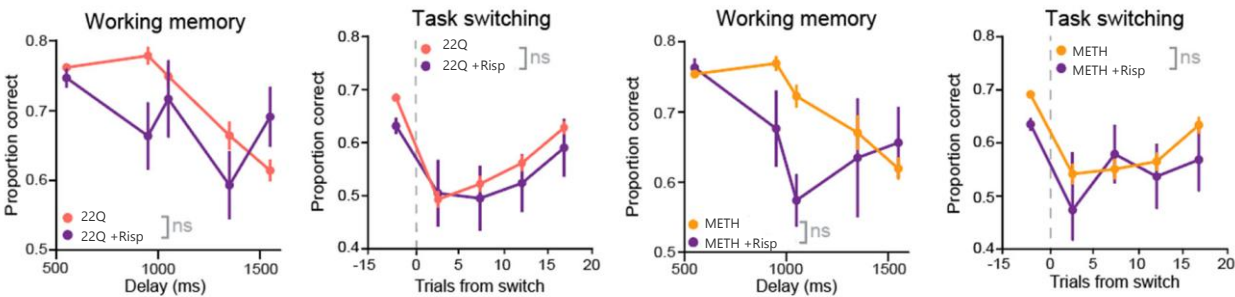
Task switching



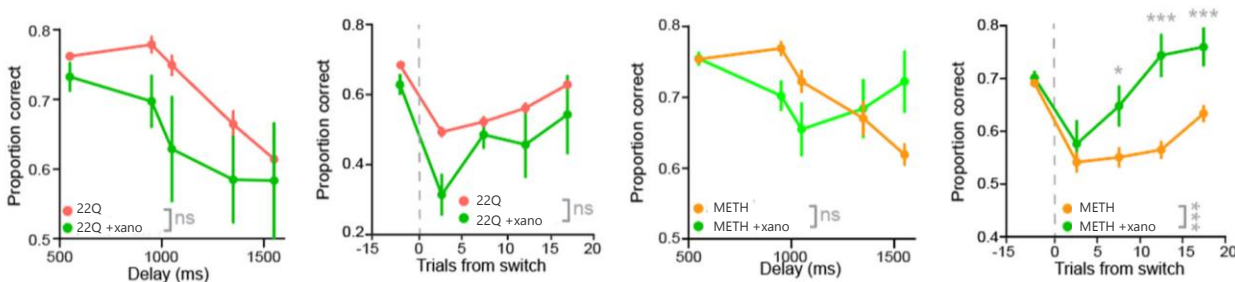
Ovid KCC2 direct activator outperformed in working memory relative to risperidone and xanomeline (Cobenfy active ingredient) and provided task switching benefit compared to risperidone

KCC2 direct activation consistently restores working memory and task switching across numerous models

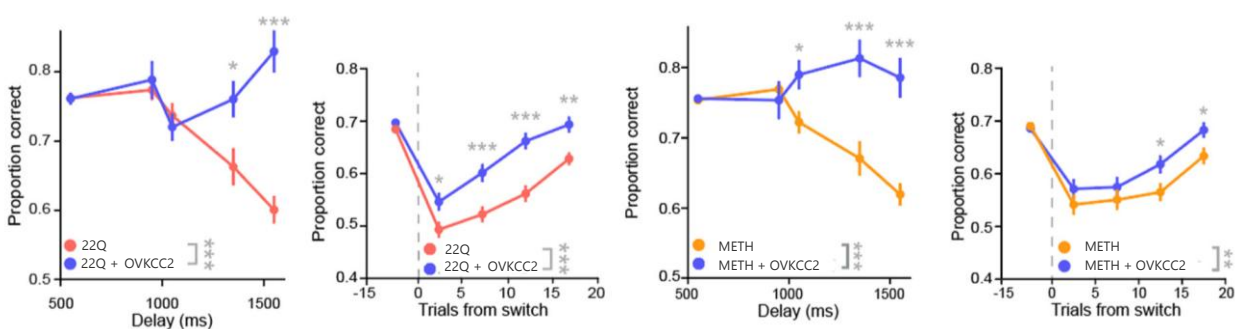
Traditional antipsychotic
D2 Receptor antagonist,
(risperidone)



First-in-class antipsychotic
M1/M4 receptor agonist,
(xanomeline/trospium)



Ovid KCC2 direct activator



CONCLUSION:

KCC2 direct activation shows broad potential for treatment of psychotic disorders

- ✓ **Excitatory/inhibitory balance is disrupted in the schizophrenia prefrontal cortex**

- ✓ **Reduced KCC2 function may be an underlying mechanism**

- ✓ **KCC2 activators have utility across genetic and pharmacological models related to schizophrenia**

- ✓ **KCC2 activation has broad utility for symptom targeting beyond positive symptoms – including cognitive function, which is correlated with negative symptoms**



OV4071: A broad potential syndromic antipsychotic

Eliseo Oeste Salinas, MD, MSc
Senior Strategic Advisor:
R&D Strategy, Ovid Therapeutics

Our vision

-  **Direct KCC2 activator**

-  **Broad potential syndromic antipsychotic (robust behavior in psychosis models)**

-  **Rescues deficits in cognition, activity in hyperlocomotion models**

-  **Commensurate-to-superior activity to xanomeline, pimavanserin**

-  **No sedation or catalepsy**

-  **Translatable electrophysiological biomarkers**

OV4071 fundamentals

Highly potent & selective



20-fold potency

in psychosis models vs OV350

0.64 μM KCC2 selectivity

Suitable for chronic dosing



13 hours

predicted half-life ($T_{1/2}$)

Orally active

Direct binding & activation



Confirmed activation

of potassium/chloride ion flux

Therapeutic index



17-fold safety margins

No relevant off-target activity

in other receptors relevant to psychosis

Potential tolerability



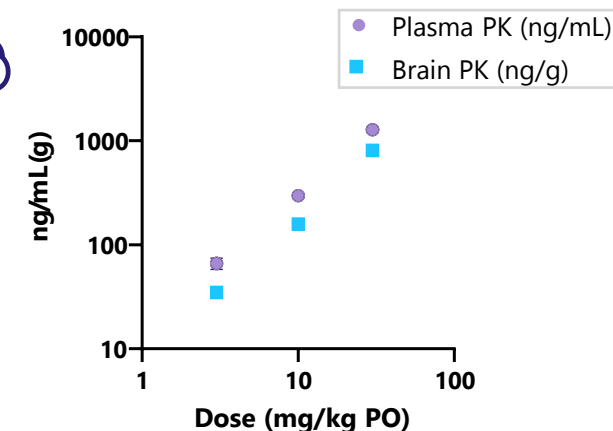
No sedation

No significant drug:drug

interactions anticipated

No catalepsy

1:1 brain-to-plasma ratio

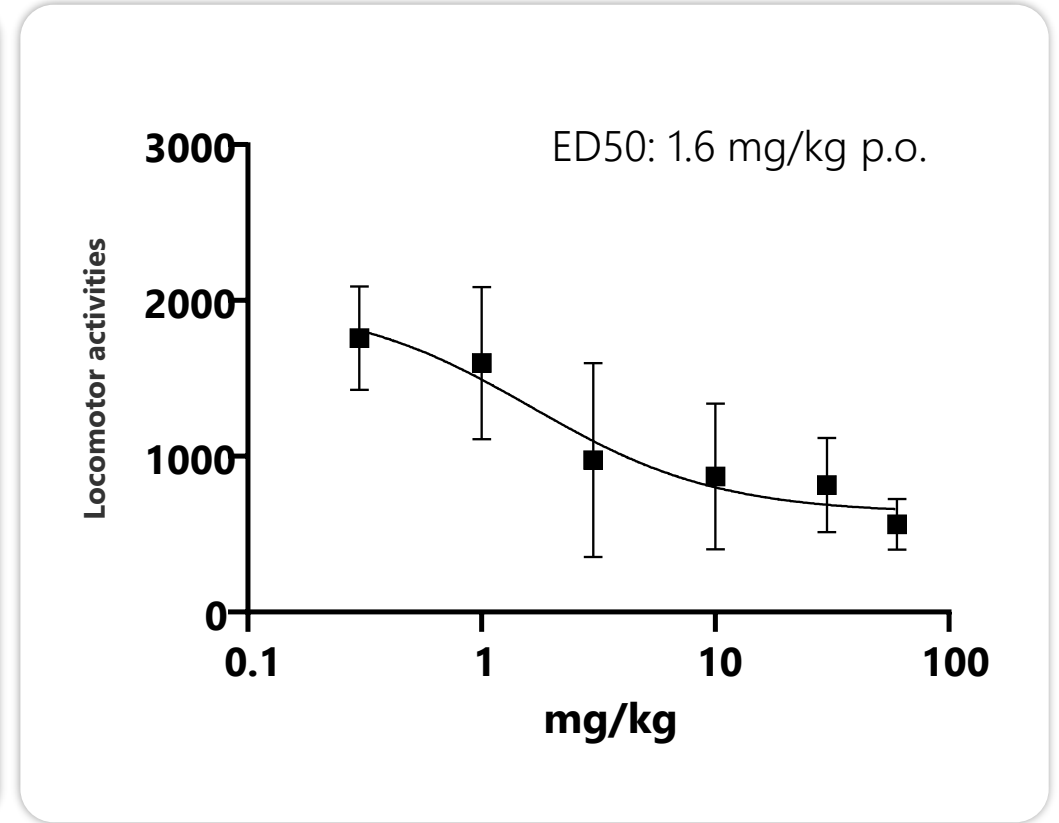
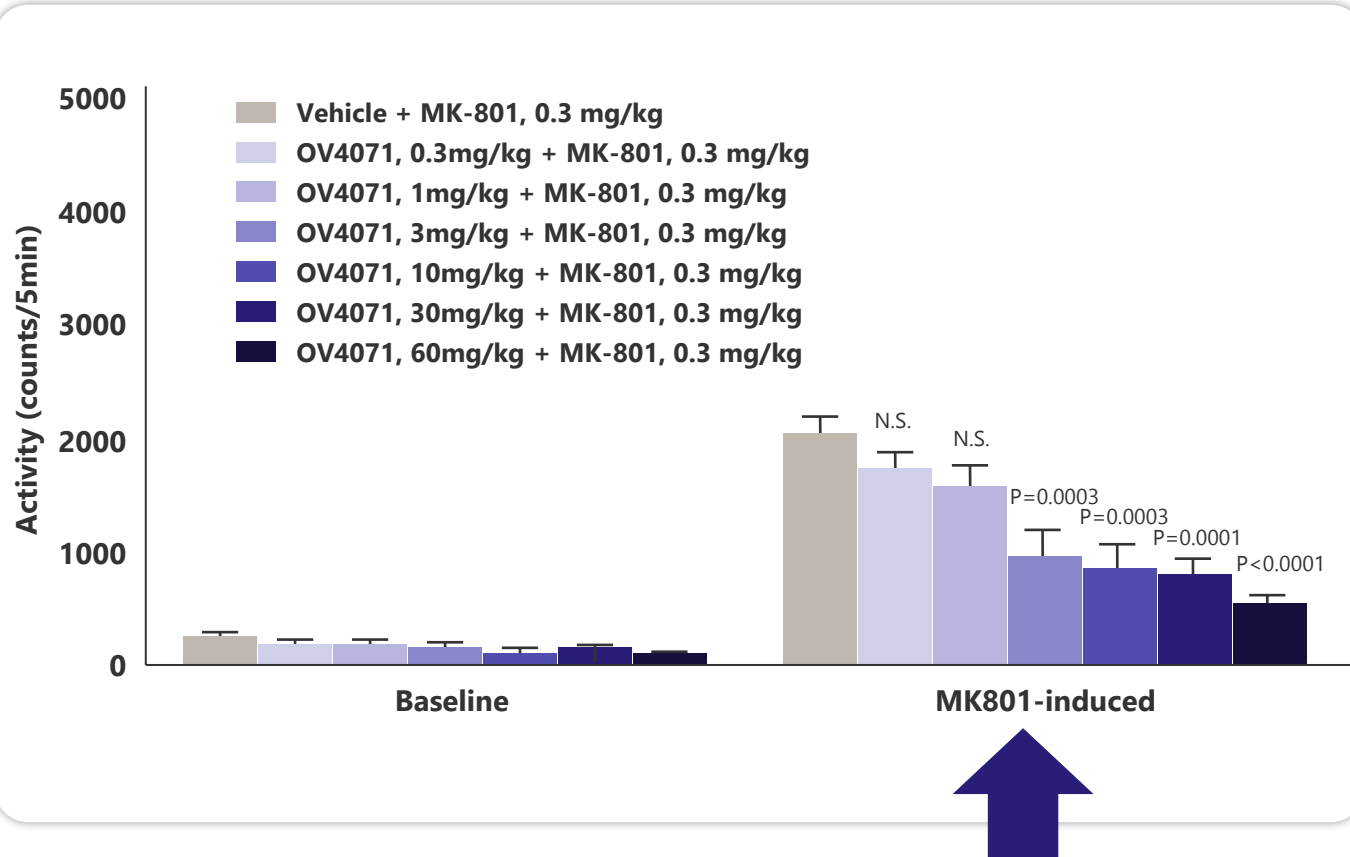


Pharmacodynamic results suggest OV4071 has broad antipsychotic effects

Model	MK801 (NMDA antagonist)	Amphetamine	Phencyclidine behavior (NMDA glutamate receptor antagonist)	MECP2 deletion
	Acute		Chronic	
Relevance	- Induces hyperlocomotion - Surges glutamate & dopamine in the striatum	- Acute model - Induces hyperlocomotion - Surges striatal dopamine	- Chronic model of negative symptoms - Suppresses social interaction - Reflects insufficient dopaminergic input in cortex	Deletes a protein abundant in mature neurons central to maintaining normal synaptic communication
OV4071 profile implications	- Rapid, sustained rescue of physiological behavior - On-mechanism reduction in dopamine	- Rescues psychosis behaviors without sedation - Demonstrated effect in models in which pimavanserin had no activity	Restores animal sociability as effectively as clozapine	- EEG biomarker activity consistent with the MoA - Shift EEG power frequencies relevant to psychosis

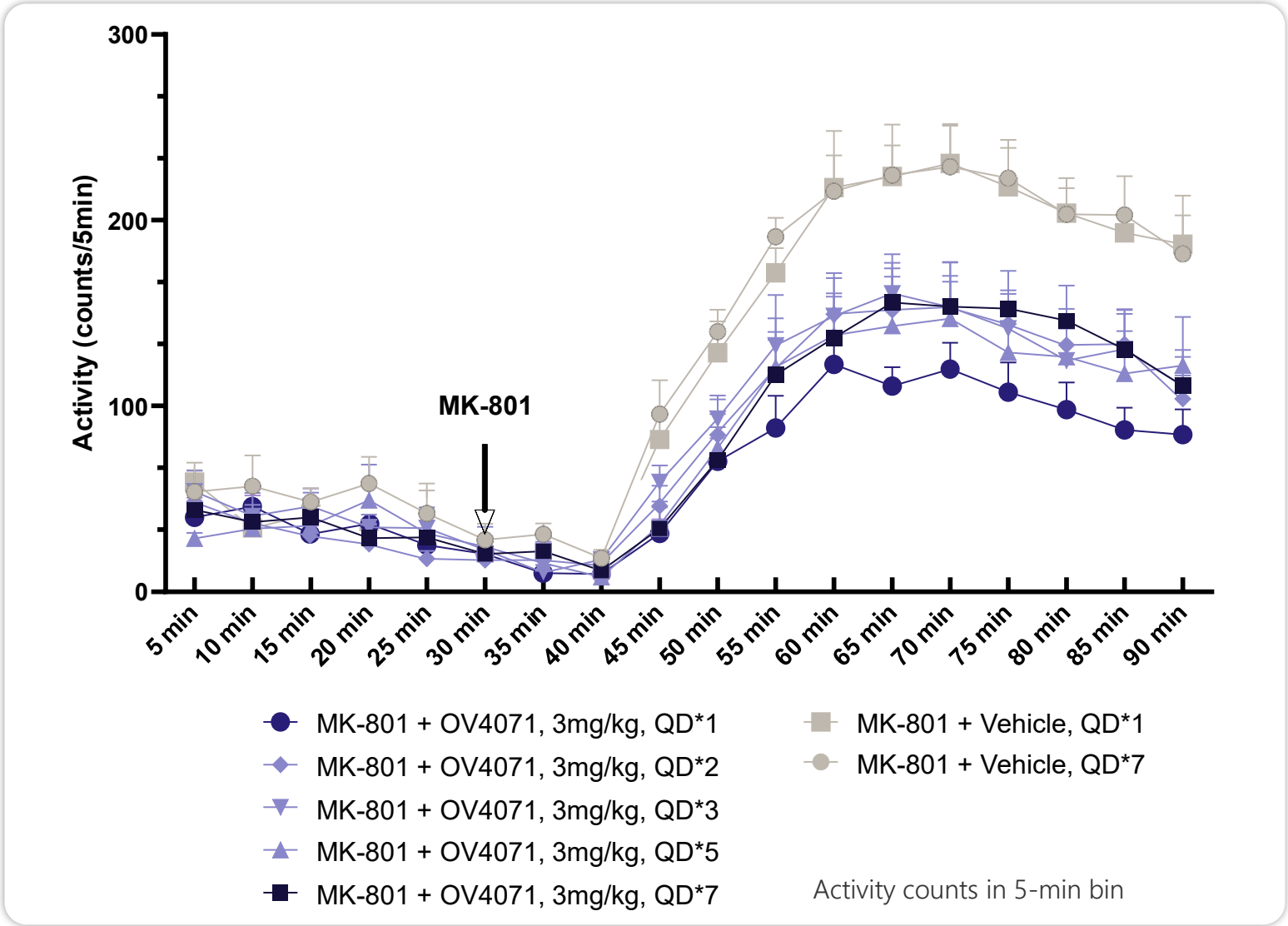
OV4071 delivers robust, dose-dependent signal in MK801 schizophrenia model

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

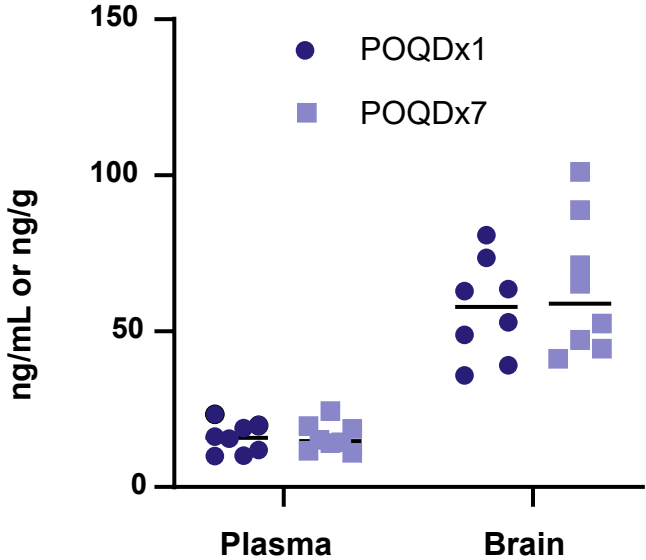


OV4071 returned locomotion to natural levels (1,500 – 2,000 counts) in a dose-dependent fashion and reduced striatal dopamine

Rapid single dose effect: maintained upon repeated administration

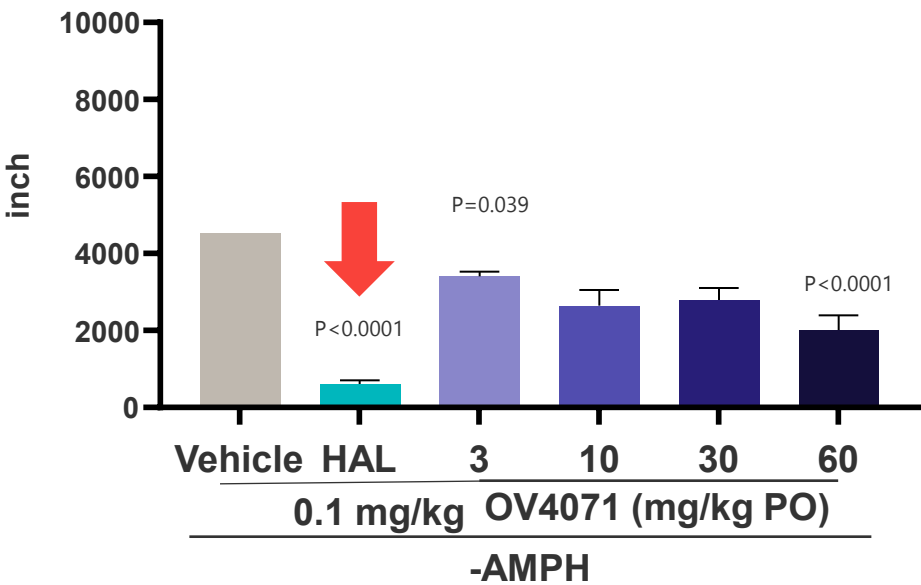


PK after single and 7xPOQD (100 min post administration)

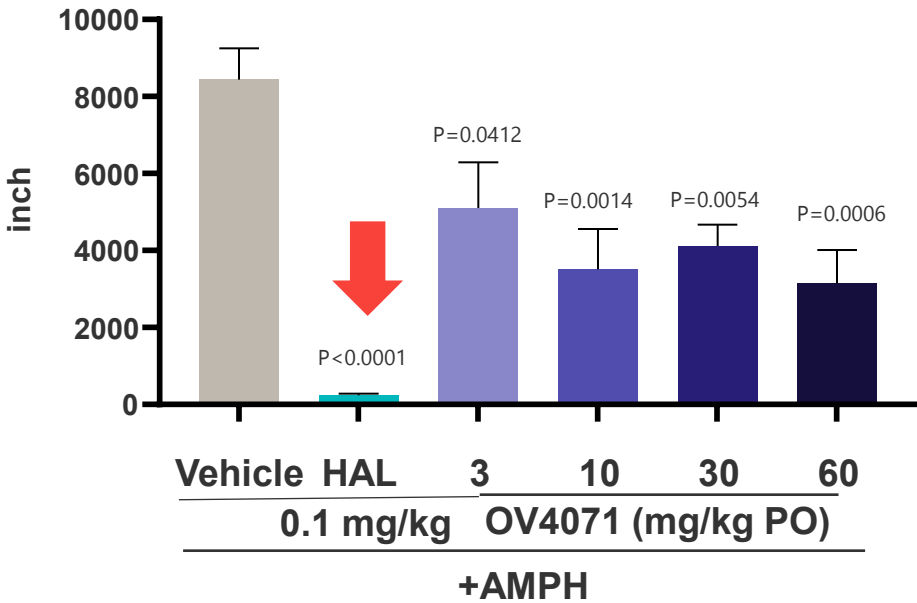


OV4071 single administration in the mouse AMPH hyperlocomotion model

Pre-amphetamine administration



Post-amphetamine administration



OV4071 was orally dosed in 0.5%HPMC/0.1%Tween80 suspension 30 min before AMPH injection (N=5-7).
Haloperidol (HAL) was injected intraperitoneally (0.1 mg/kg)

**Post-amphetamine stimulant, OV4071 reduces hyperlocomotion,
while maintaining normal physiological movement**

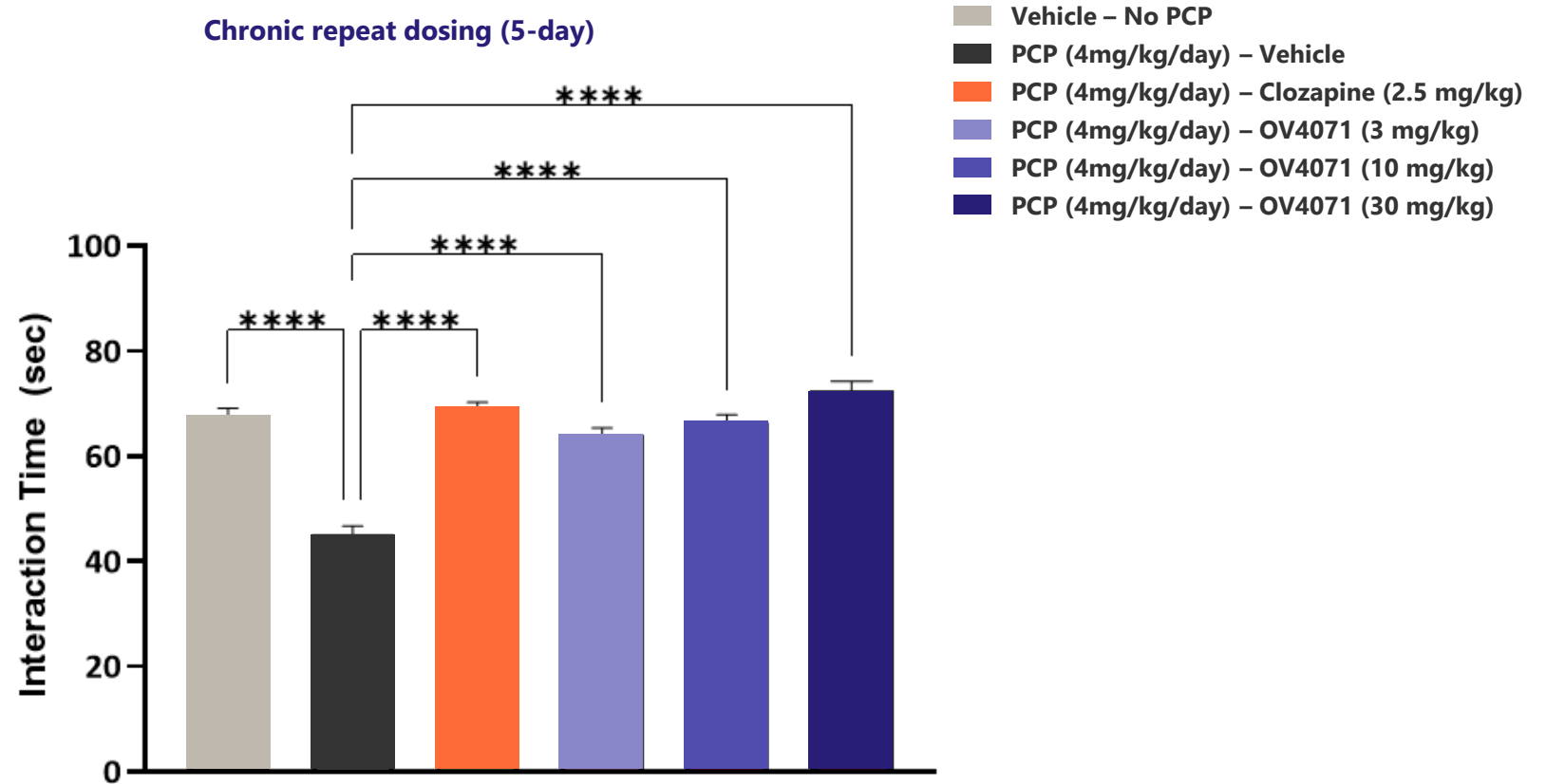
OV4071 restores social interaction in chronic PCP-induced animal behavior model

Methods

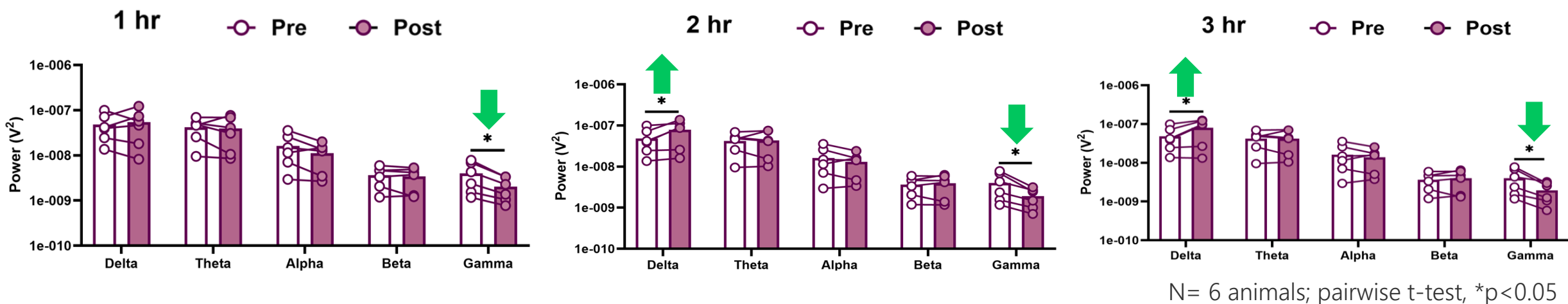
Induce asociality and reduced interactions with phencyclidine

Results

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



OV4071 demonstrated translationally relevant biomarkers



Methods

Recovery	Baseline	OV 4071 7.5mg/kg (i.p.)
1-week	2-hours	3.5 hours

- Low dose of KCC2 (7.5 mg/kg) on baseline EEG power in Rett (MeCP2) mice
- Comparisons were made with the pre-treatment period

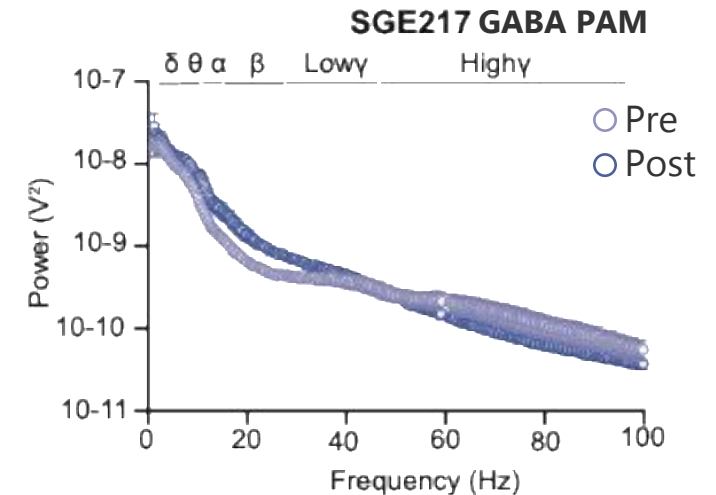
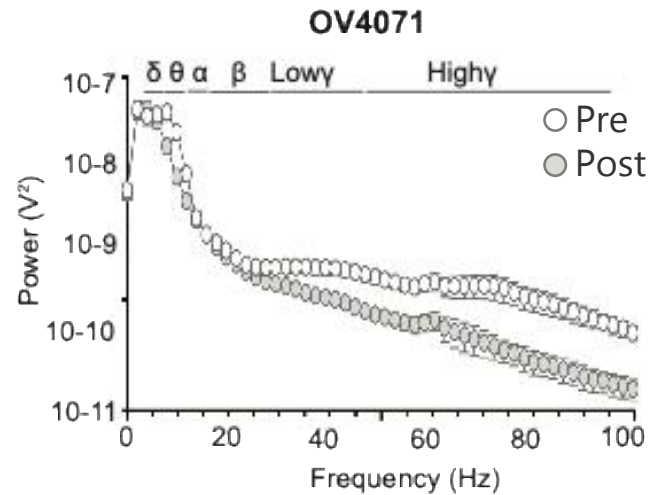
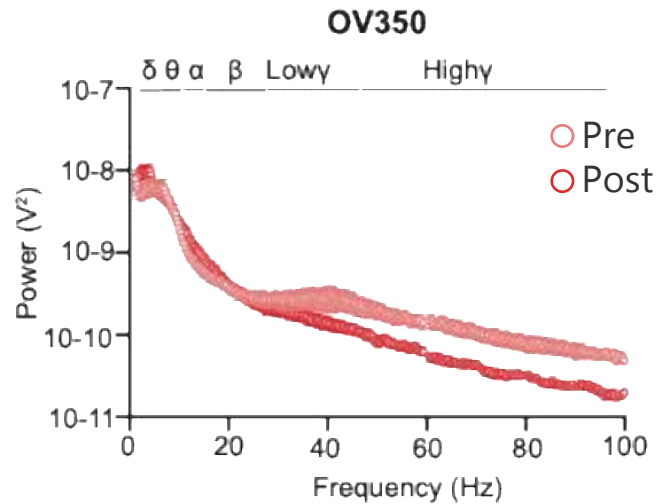
Results

- Rapid reduction in Gamma observed 1-hour post-dose
- Delta power increases

Implications

- Gamma increased is schizophrenia at rest, so reductions are suggestive of activity
- Delta power increases suggesting synaptic signaling restoration

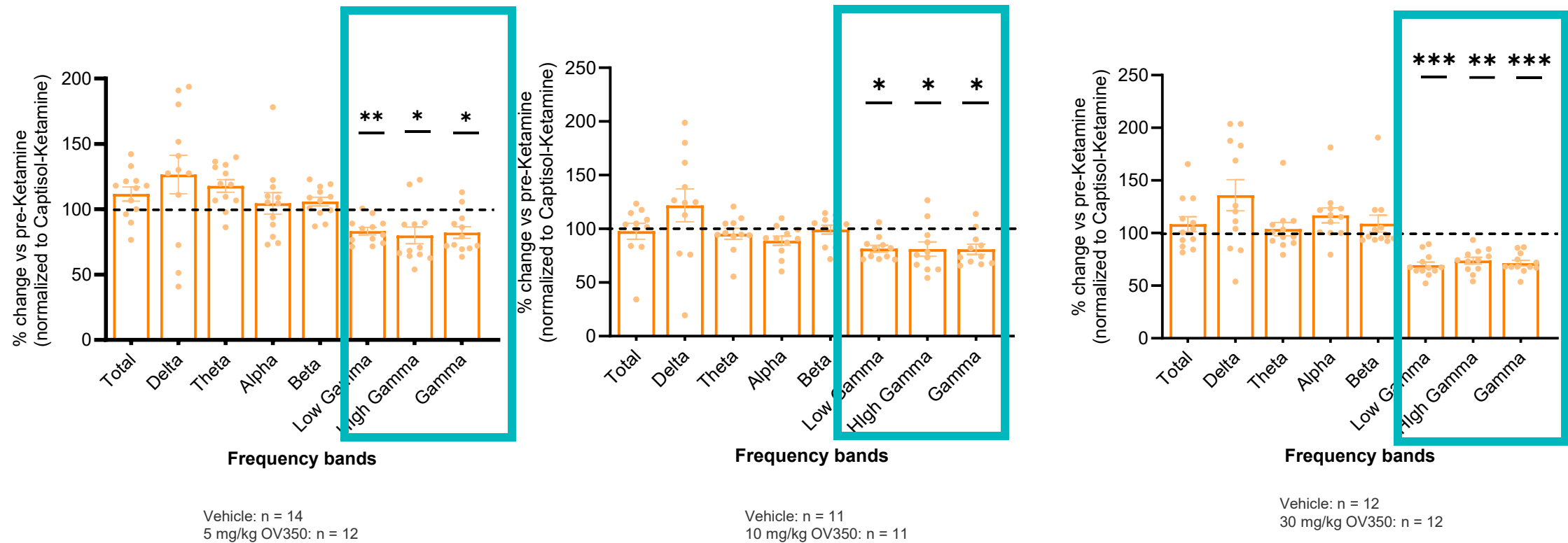
KCC2 activators share a pharmacodynamic profile that is clearly distinguished from drugs that directly enhance GABAergic activity



- SGE217 (Zuranolone) a positive allosteric modulator of GABA_A receptors induces a robust increase in beta power (13-30 Hz)
- Ovid KCC2 direct activators increase low frequencies and decrease gamma at rest

OV350 restores qEEG signals induced by ketamine in mice

EEG frequency changes in mouse ketamine challenge study (OV350 varying doses)



OV4071: **A broad potential syndromic antipsychotic**

Robust behavior in multiple stimulant, glutamatergic/dopaminergic disease biology models

- Restores typical animal physiological activity
- Restores social behavior (interaction time) comparable to clozapine

Highly potent effect at single and repeat doses

- Speed of effect is rapid (<1 hour)

Reduces striatal dopamine levels consistent with mechanism of action

Biomarker activity consistent with mechanism of action

Strong brain-to-plasma penetration

Not sedating

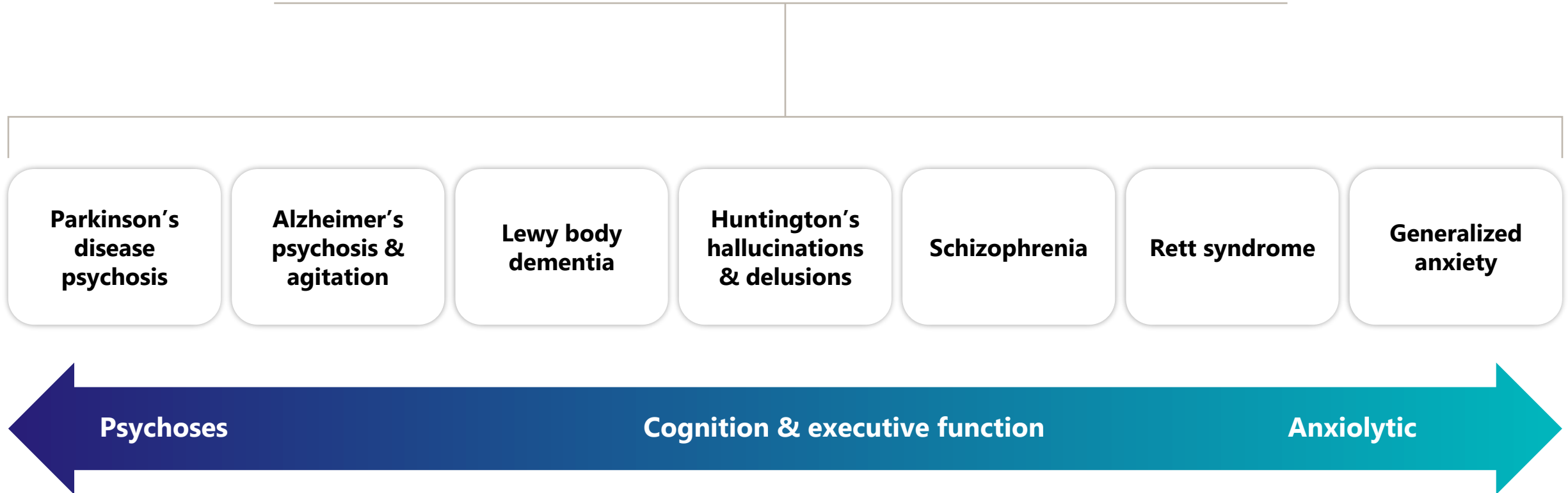


Translational and clinical strategy

Meg Alexander, President & Chief Executive Officer
Ovid Therapeutics

The OV4071 opportunity:

Broad applications in syndromic psychosis & psychiatric disorders



Translational strategy

Pharmacodynamic activity characterization in phenotypic and in vivo models

- Genetic models
 - Stimulant induced models
 - Reference drug comparators
 - Suggestive/predictive electrophysiology
-

Broad electrophysiology biomarkers in healthy volunteers

Broad and indication-relevant electrophysiology biomarkers in stimulant induced humans (ketamine, an NMDA antagonist)

Electrophysiology and clinical symptom evaluation in patient signal finding and proof of concept studies

Establish a consistent “red thread” through animal pharmacology, human and patient studies

Phase 1 tool program results support KCC2 development

Objective & design

Exploratory randomized, placebo-controlled, single-ascending dose study in healthy volunteers

- 16 participants (6=active, 2=placebo per cohort)
- Doses 50 mg and 100 mg
- Formulation: IV infusion

Measured

- Safety, tolerability, PK
- Exploratory electrophysiology

Good safety profile; no:

- Treatment-related laboratory findings
- Treatment-related serious adverse events

Most common AEs were headache, GI disturbance

Pharmacokinetics were as predicted

Achieved C_{max} significantly over projected EC₅₀

qEEG biomarker suggestive of central activity

- Spectral power shift consistent with KCC2 modulation
- Gamma band changes
- Aligned with drug exposure in brain

Phase 1 SAD/MAD study design

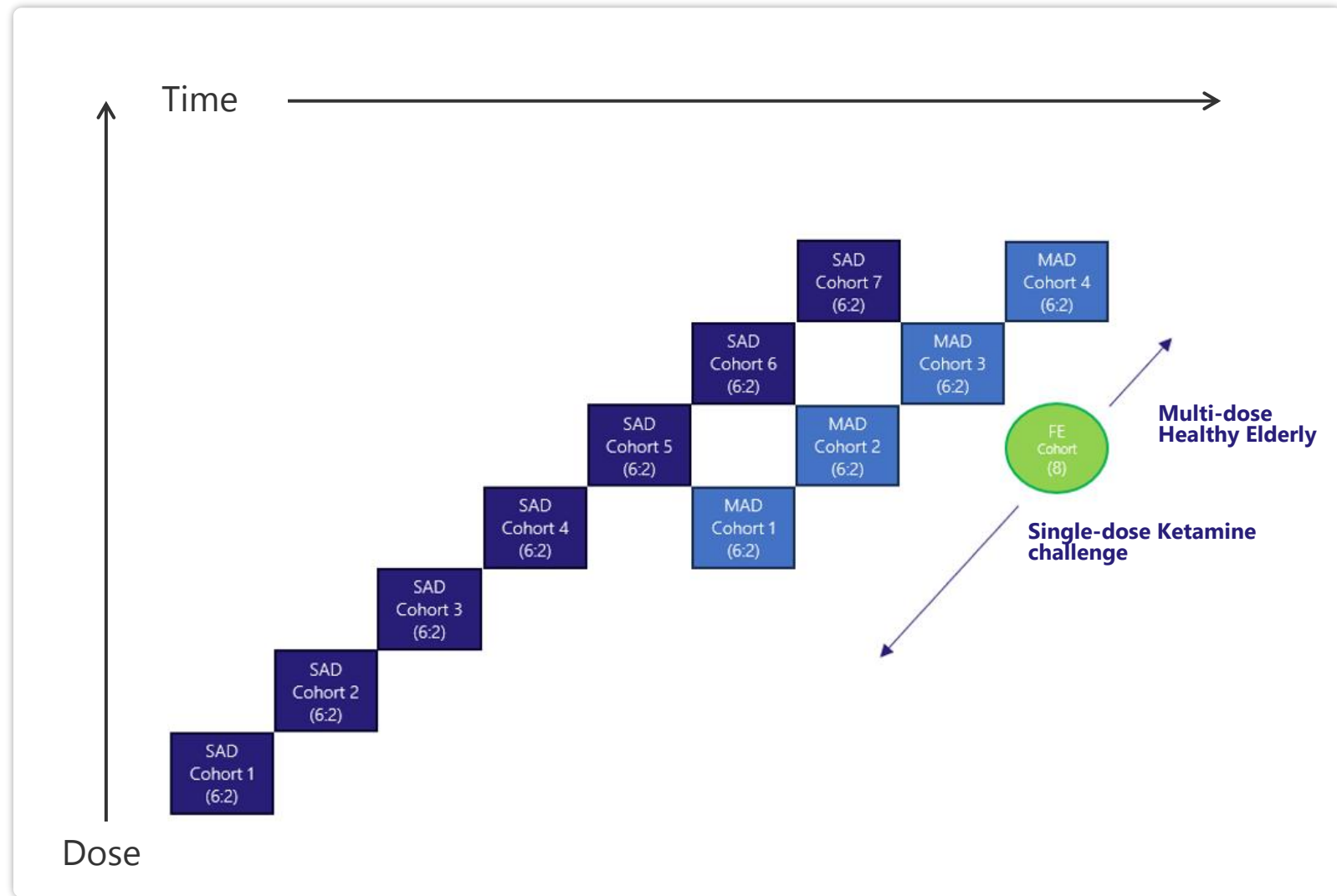
Healthy volunteer SAD/MAD

Endpoints:

- Safety and tolerability
- Pharmacokinetic profile
- Pharmacodynamic biomarkers
 - Quantitative EEG
 - Event-related potentials (ERPs)
- Food effect cohort in parallel

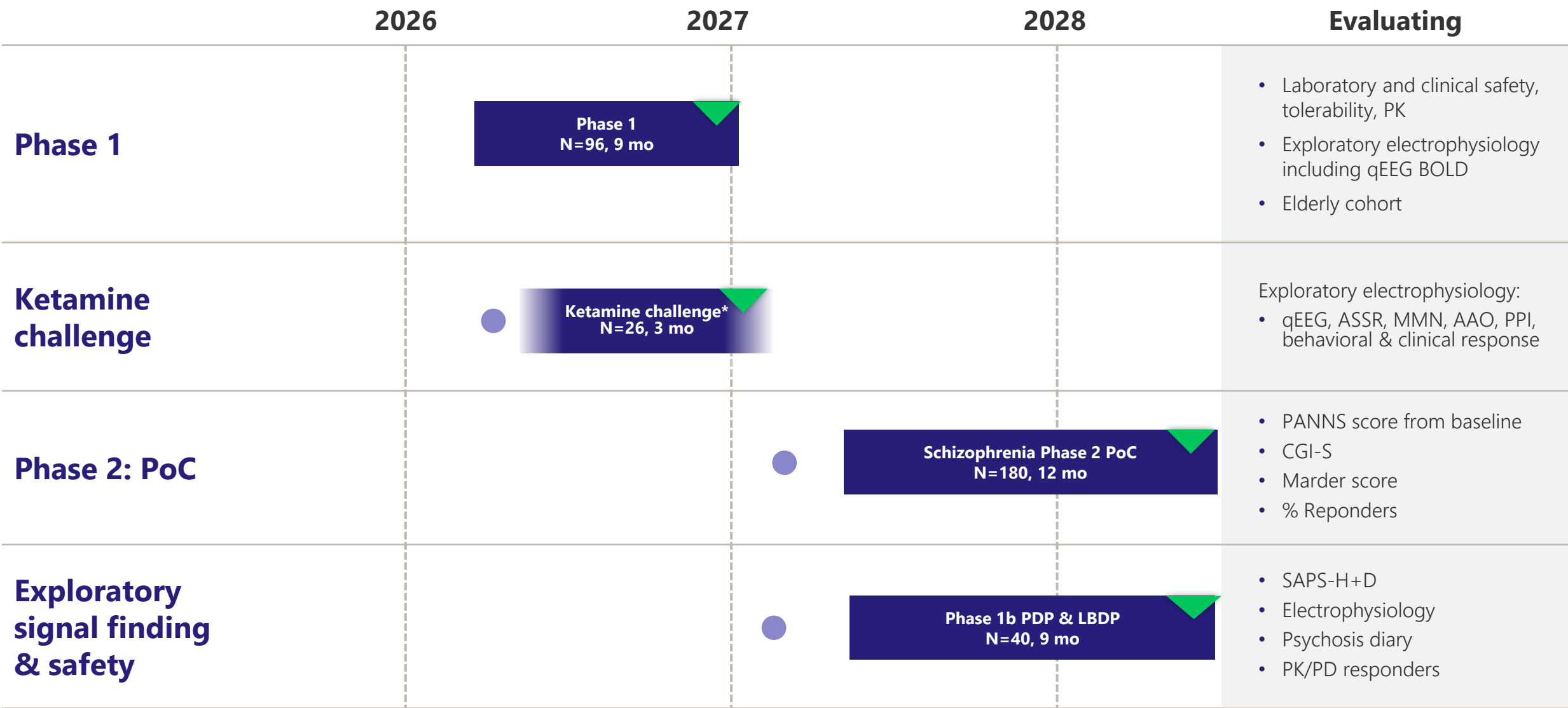
Ketamine challenge target engagement study in parallel to SAD

Healthy elderly safety cohort



Robust translation & clinical characterization

- Regulatory interaction
- ▼ Data availability



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

Electrophysiology biomarkers leveraged in Phase 1

Electroencephalography (EEG) and event-related potential (ERP) biomarkers

Biomarker	Relevance	Measure
Quantitative EEG (qEEG)	Arousal and activation	- Absolute and relative spectral power (uV) in traditional frequency bands - Slope of aperiodic (non-oscillatory) component
Active Auditory Oddball	Cognitive processing speed and resource allocation	- Amplitude of early sensory-evoked (N100, P200) - Amplitude and latency of P300b
Mismatch Negativity	Automatic encoding and detection of change in sensory scene	- MMN amplitude measured in difference wave of standard-deviant conditions - P3a amplitude evoked by deviant stimuli
Auditory Steady State Response	Neural synchrony	- Evoked spectral power (uV) in gamma (30-50 Hz) - Phase consistency measured by intertrial coherence
Prepulse Inhibition	Auditory sensory gating	% change in amplitude of auditory-evoked response to “pulse” stimuli

ELECTROPHYSIOLOGY STRATEGY:

Relevance in schizophrenia

Electroencephalography (EEG) and event-related potential (ERP) biomarkers

Biomarker	Relevance in schizophrenia	Biomarker changes
Quantitative EEG (qEEG)	Hypo-frontality pattern associated with negative symptoms and cognitive dysfunction	• Δ low-frequency power (delta and theta) • Reduced alpha power, primarily in the frontal lobes • Δ to gamma power
Active Auditory Oddball	Impaired attentional allocation and working memory updating Deficits present in clinical high-risk and first-episode patients, and continue to progress with disease chronicity	• Δ latency and decreased amplitude of P300 response
Mismatch Negativity	Implicates NMDA hypofunction Associated with higher symptom severity and functional impairment Predictive of conversion to psychotic disorder in clinically high-risk patients	• Lower MMN amplitude in difference wave • Low P3a amplitude in response to deviant stimuli
Auditory Steady State Response	Associated with clinical symptom severity (hallucinations, psychotic severity, and cognitive decline) Predictive of conversion to psychotic disorder in CHR samples	• Lower evoked spectral power and phase-locking / coherence
Prepulse Inhibition	Reduced sensory gating capacity is a trait-marker of sensory input dysfunction	• Lower PPI ration (less suppression)

qEEG: Gattaz et al. *Eur Arch Psychiatry*1992; AOD: Hamilton et al. *Schizophr Bull.* 2019; MMN: Nagai et al. *Front. Psychiatry*2013; ASSR: Sugiyama et al. *Front. Psychiatry* 2021; PPI: Swerdlow et al. *Schizophr Res.* 2018

ELECTROPHYSIOLOGY STRATEGY:

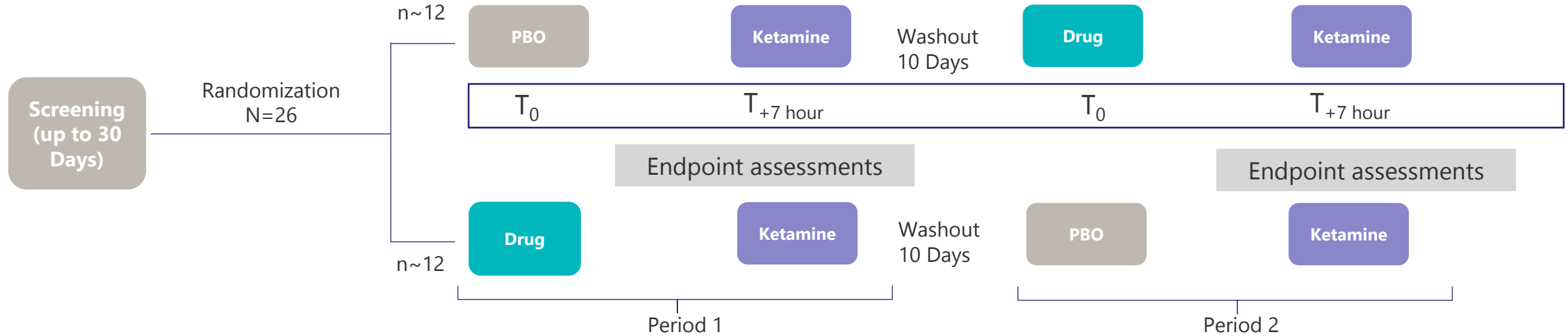
Parkinson's disease psychosis (PDP)

Electroencephalography (EEG) and event-related potential (ERP) biomarkers

Biomarker	Relevance in PDP	Changes
Quantitative EEG (qEEG)	In PD characterized by increased slow wave (delta – theta) activity, coupled with reduced alpha - beta reactivity Progresses with disease, associated with cognitive dysfunction, hallucinations, and dementia PDP found to have higher intra-hemispheric coherence in beta and gamma bands than PD non-psychosis	• Δ progressive “slowing pattern”
Active Auditory Oddball	Associated with longer reaction time in response to targets and smaller P300 amplitude compared to PD non-psychosis correlates with attention and working memory test performance	• Δ latency and decreased amplitude of P300 response
Mismatch Negativity	Visual MMN is significantly reduced or absent in PD patients experiencing visual hallucinations compared to those without	• Δ to amplitude of P2a response to deviance
Auditory Steady State Response	Data on ASSR in PDP is limited; though 40 Hz is increasingly used as a biomarker of dementia	• Δ in ASSR (40 Hz)
Prepulse Inhibition	PPI is reduced in PD and pre-clinical models of PDP PD patients exhibit reduced PPI of the N1/P2 component in auditory cortex tests	• Δ in PPI

qEEG: Gattaz et al. *Eur Arch Psychiatry*1992; AOD: Hamilton et al. *Schizophr Bull.* 2019; MMN: Nagai et al. *Front. Psychiatry*2013; ASSR: Sugiyama et al. *Front. Psychiatry* 2021; PPI: Swerdlow et al. *Schizophr Res.* 2018

Translational study: ketamine challenge in healthy volunteers



Trial design

- Single site study in the US (Biotrial)
- Healthy volunteers 18 - 55 years of age
- Cross-over design with single dose of OV4071 vs PBO

Key Endpoints

- Resting quantitative EEG
 - Power spectral analysis of waking EEG (1-70 Hz)
- Event-related potentials (ERPs)
 - ASSR (40 Hz entrainment), P300 (active oddball), MMN (passive oddball)
- Cognitive testing, psychotomimetic effects (CADSS, BPRS)
- Plasma Biomarkers (GABA, Glu, BDNF, cytokines, ketamine metabolites)

Patient studies with OV4071

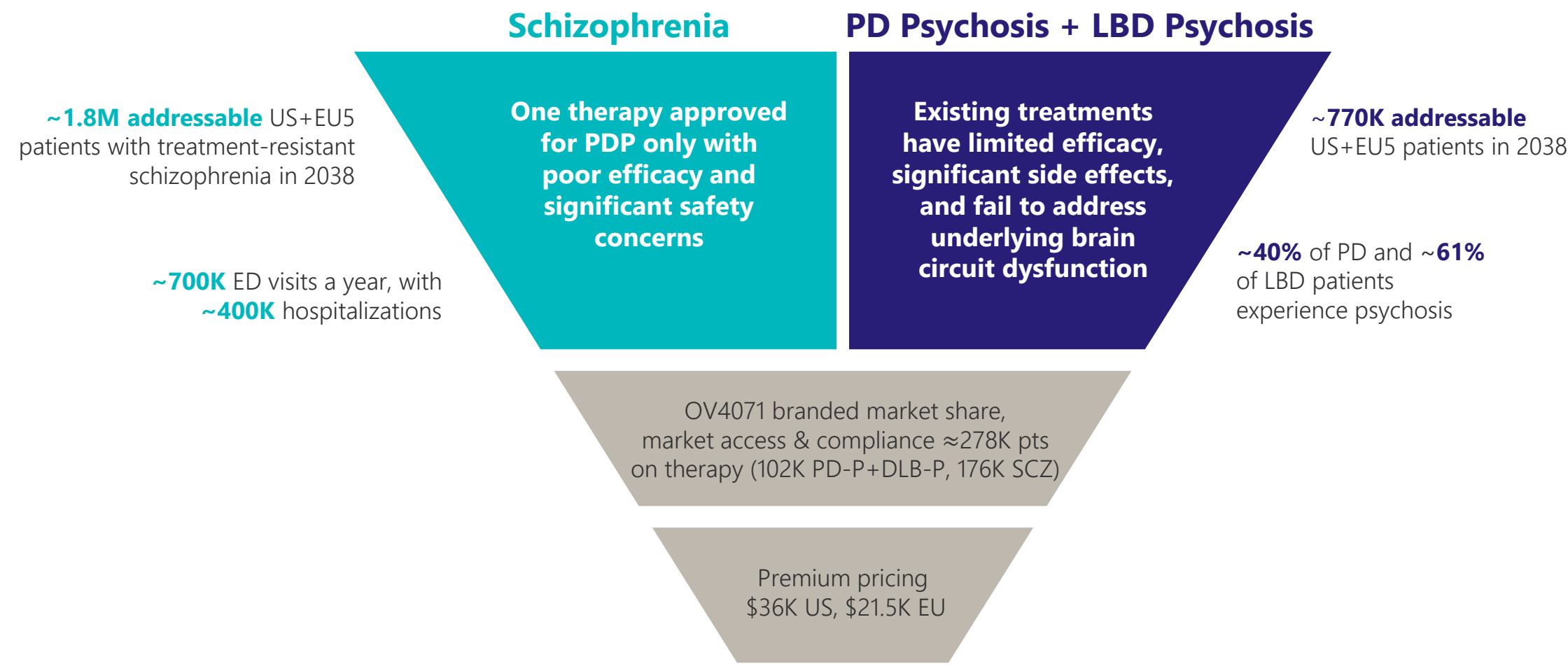
Phase 2 proof of concept in schizophrenia

- Randomized, double-blind, placebo-controlled study in patients with acute schizophrenia
- Evaluate safety, tolerability, and efficacy
- Multi-site study in US

Phase 1b exploratory signal finding & safety in PDP & LBDP

- Single arm, open-label study with titration up to two doses in patients with Parkinson's disease psychosis and Lewy body dementia psychosis
- Evaluate safety, tolerability, and exploratory clinical effect in psychosis
- Multi-site study in US

A meaningful market for OV4071

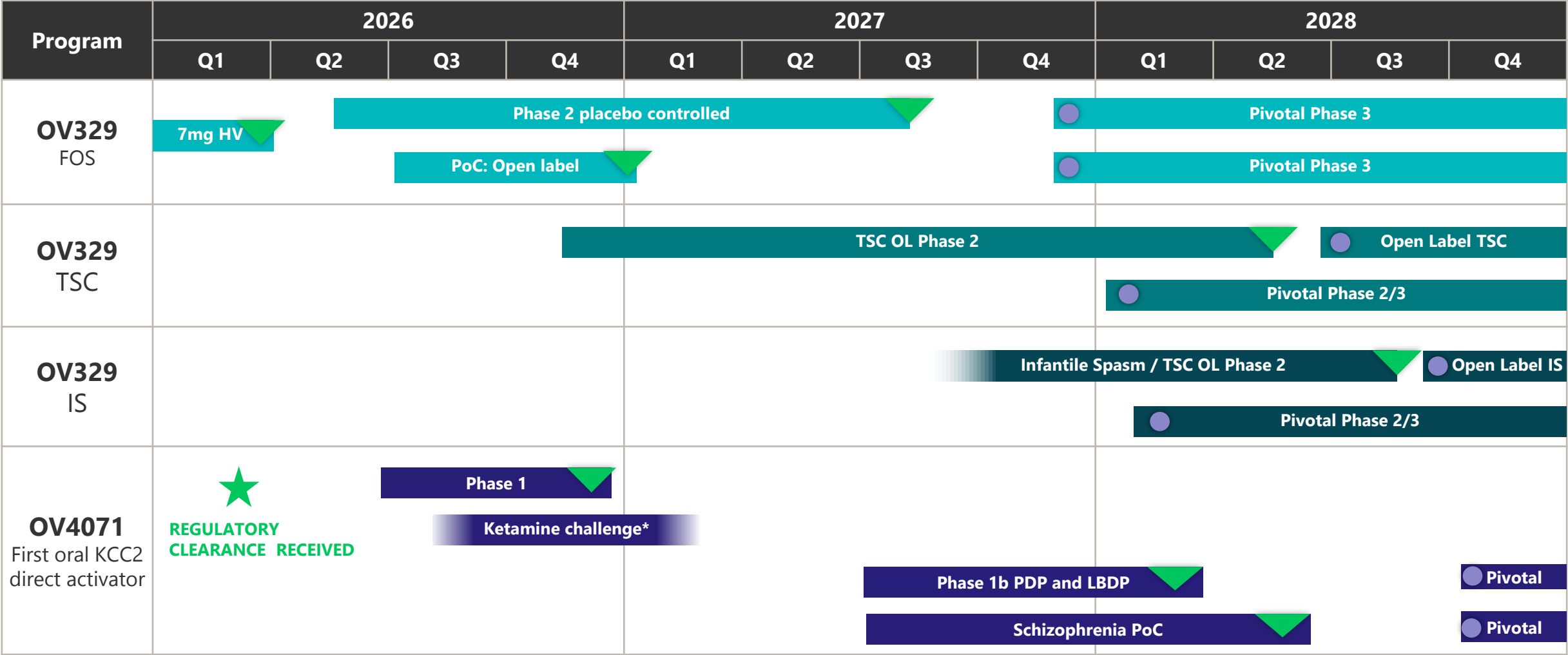


~\$6.8 Billion Peak US + EU5 Revenue in 2038

Estimates for peak OV4071 revenue in 2038; LifeSci Consulting

A milestone rich runway

 Pivotal and OLE trials that would require funding post PoC
 Data availability



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**

Pioneers of KCC2 direct activation



**One mechanism:
infinite possibility**



**Safely drugged
KCC2 with signs
of GABAergic
activity (OV350)**



**Oral program
rapidly advancing
to the clinic
(OV4071)**



**Translational
biomarkers to
inform profile &
indications**



**Discovery engine
of unique,
next-generation
activators**



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