Ovid Therapeutics

Business and pipeline update

March 18, 2026

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 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 readouts 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, OV4041 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 exercise of the warrants issued in the October 2025 private placement financing and the aggregate proceeds payable to Ovid should all holders of Series A Warrants choose to exercise their warrants; the intended use of the proceeds from the private placement announced on March 18, 2026, including for the development of OV329 in additional indications including tuberous sclerosis complex seizures and infantile spasms; 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, impediments to Ovid's ability to achieve expected benefits of cost-savings efforts, 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 business strategy, and the holders of the warrants issued in the October 2025 private placement may choose not to exercise the warrants prior to their expiration and the price targets that would permit Ovid to require certain of the warrants to be exercised may not be achieved. 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.

New business highlights

Pipeline

Received regulatory approval to initiate Phase 1 study of 1st- ever, oral KCC2 direct activator, OV4071*

7 mg dose OV329 GABA-aminotransferase inhibitor demonstrated strong safety and tolerability profile, no treatment-related SAEs or AEs

All programs advancing on-track into patient proof-of-concept studies with anticipated readouts throughout H2 2026 - 2027

Launching additive studies for OV329 in infantile spasms and tuberous sclerosis complex seizures

Business

Announced PIPE financing led by Point72 to support new OV329 development path

OV4071 Phase 1 clearance triggers a 30-day period for the Company's Series A warrants with potential proceeds up to $53+ million***

With completion of PIPE and assuming full exercise of series A warrants, cash runway expected into 2029

*Approval granted by the Human Research Ethics Committee and the Australian Therapeutic Goods Administration

**Entered into a securities purchase agreement for a private investment in public equity ("PIPE") financing that is expected to result in gross proceeds of $60 million to the Company, before placement agent fees and offering expenses. The PIPE financing is expected to close on or about March 19, 2026, subject to satisfaction of customary closing conditions.

*** If exercised in full. Does not reflect placement agent fees

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, sequential clinical & regulatory milestones anticipated throughout H2 2026 - 2027

High-value, differentiated pipeline

	Programs	Potential Opportunity	Preclinical	Phase 1	Phase 2	Anticipated milestones*
	OV329, a next-generation GABA-aminotransferase (AT) inhibitor					
New programs	**Drug-resistant adult focal onset seizures (FOS)**	Distinct mechanism of action in FOS with: • Competitive efficacy • Superior tolerability & safety • No expected titration or drug:drug interactions	**Phase 2 RCT** **Open label photo paroxysmal response proof-of-concept**			• Phase 2 initiation (Q2 2026) • Open-label photo paroxysmal response (PPR) initiation and results H2 2026 • Phase 2 topline results (mid-2027)
New programs	**Tuberous sclerosis complex seizures (TSC)**	1st approved GABA-AT inhibitor • Preferable safety, tolerability • Increased treatment duration	**PoC & safety**			• PoC safety and signal finding study to initiate in Q4 2026
New programs	**Infantile spasms (IS)**	Disease modifying first-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)					
Now cleared	**Broad spectrum psychosis**	• Psychosis associated with Parkinson's disease and Lewy body dementia • Acute schizophrenia **Additional indications:** • Neurodegenerative psychoses • Other undisclosed indications	**Phase 1** **Ketamine challenge w/biomarkers**			• Phase 1 initiation (Q2 2026) • Proof-of-mechanism ketamine study (initiation H2 2026) • Phase 1b PoC studies & results (H2 2026 - 2027)

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

OV329, a potential best-in-category anti-seizure medicine for treatment-resistant & developmental epilepsies

NEW UPDATES

Clinical progress & indication expansion

Focal onset seizures

7 mg dose well tolerated with no treatment-related SAEs or AEs in healthy volunteers

5 mg and 7 mg doses deliver target drug exposure in the plasma, favorable tolerability and predictable, linear pharmacokinetics (PK)

On track to initiate:

- Phase 2 randomized controlled, dose confirmatory trial in treatment-resistant focal onset seizures
- Anti-convulsant proof-of-concept open label seizure study in photo paroxysmal seizures

ADDED PROGRAMS

Infantile spasms & tuberous sclerosis complex seizures

Pursuing proof-of-concept studies in tuberous sclerosis complex seizures & infantile spasms

OV329 offers a differentiated, potentially safer profile than standard of care (SoC); enabling earlier and longer use

Potential for orphan status and efficient path to registration

OV329 offers a potential best-in-category anti-seizure medicine profile

Quell hyper-excited neurons by optimally tuning synaptic and extra-synaptic GABAergic inhibition

Potent, lower dosing
(est. OV329 human doses:
5-7 mg vs 2,000-3,000 mg for VGB)

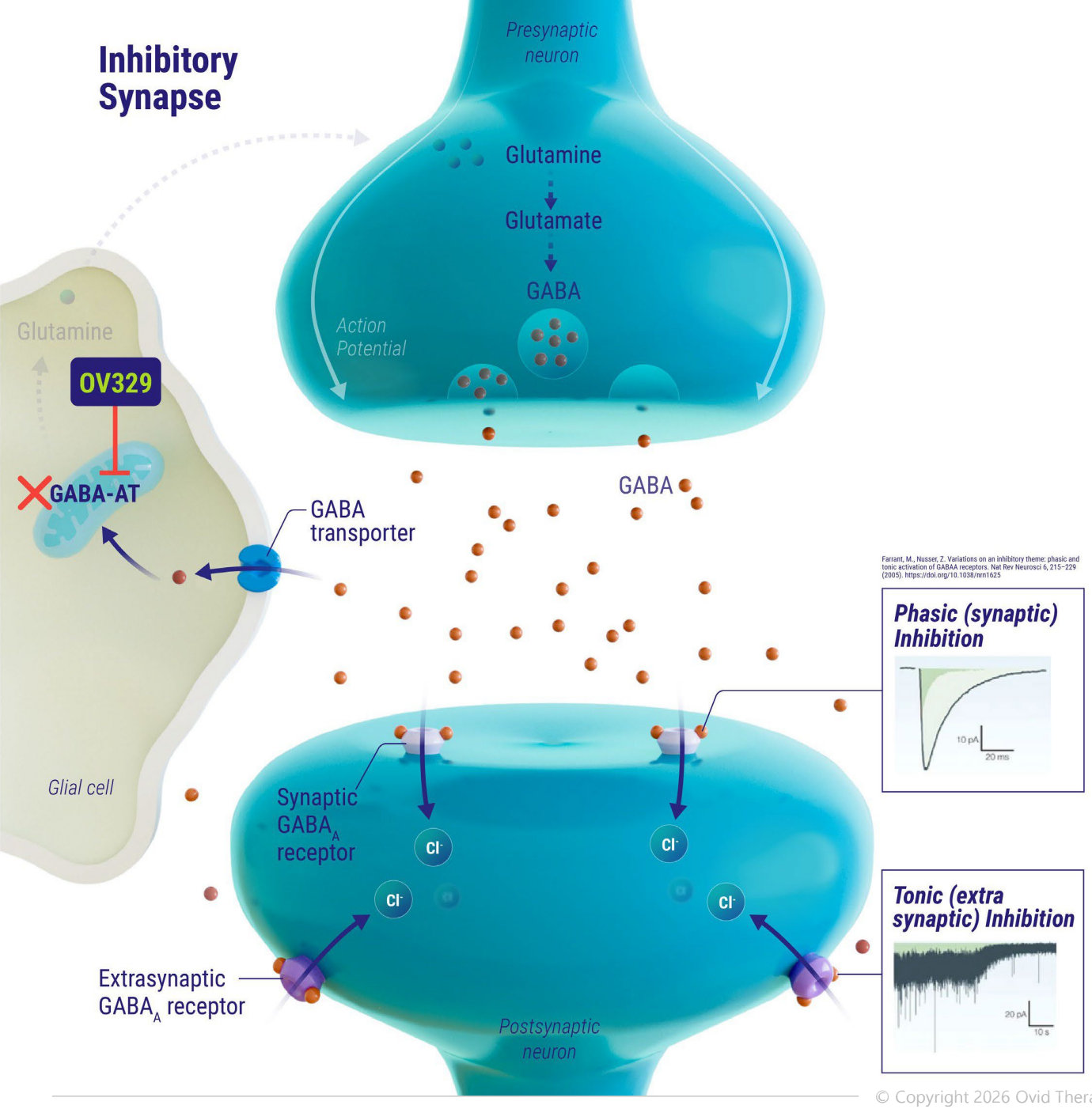
Oral, once daily dosing

Best-in-category tolerability
(no treatment-related or treatment emergent adverse events associated with OV329 7 mg in Phase 1 participants)

Competitive seizure reduction efficacy and potential best-in-category safety profile
(predicted)

No titration anticipated

Advancing to multiple proof-of-concept studies



OV329: believed to optimally tune GABA & enhance tolerability & efficacy

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

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

Creates an inhibitory neural environment that averts the tolerability issues associated with surging GABA in the synapse

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

The OV329 opportunity:
A universal mechanism for treatment resistant seizures

ONGOING

Capsule formulation (adult)

Indication
Adjunctive therapy for focal onset seizures (FOS)

Prevalence*
15 million adults with uncontrolled FOS worldwide

Validated mechanism in FOS
1st generation drug, vigabtrin (SABRIL) used last line due to compound specific ophthalmic safety

NEW EXPANSION

Pediatric weight-based

Indications
Tuberous sclerosis complex associated seizures (TSC)

Infantile spasms (IS)with clinical spasms and hypsarrhythmia

Prevalence*
TSC: 41,000 in the U.S. and EU5

IS: 14,000 in the U.S. and EU5

Validated mechanism in IS & TSC
IS: 1st generation drug, vigabatrin (SABRIL) used 2nd line & for short duration due to ophthalmic safety

TSC: Vigabatrin (SABRIL) used in limited treatment duration due to ophthalmic safety concerns

*CDC https://www.cdc.gov/epilepsy/data-research/facts-stats/index.html; Kobau et al., 2024 https://pubmed.ncbi.nlm.nih.gov/38820685/; Ioannou et al., 2022 https://pmc.ncbi.nlm.nih.gov/articles/PMC9480957/; WHO https://www.who.int/news-room/fact-sheets/detail/epilepsy

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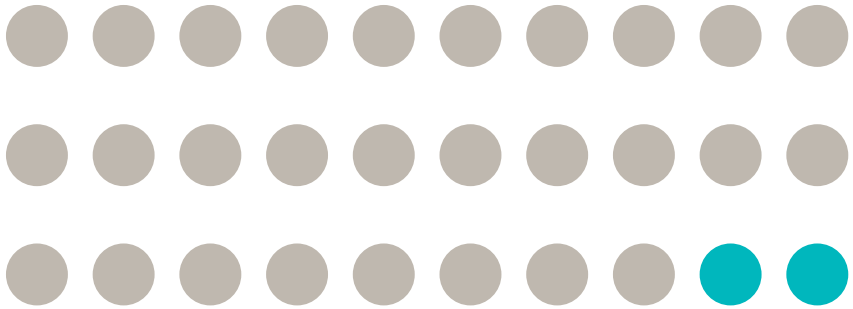
New mechanisms of action are needed in focal onset seizures

Drug resistant epilepsy (DREs)

30 anti-seizure medications approved in 15 years, but only 2 with novel mechanisms[1]



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

47% of epilepsy patients in the U.S. report poly-pharmacy use taking 5 medications on average[2]

1. Each dot = 1 FDA-approved anti-seizure medications (ASMs); Blue dots are Fycompa and Cenobamate
2. Terman SW, Aubert CE, Hill CE, et al. Polypharmacy in patients with epilepsy: a nationally representative cross-sectional study. Epilepsy Behav. 2020;111:10726

NEW FINDINGS

7 mg dose in adults further demonstrates potential favorable safety and tolerability profile

Objective

Evaluated safety and tolerability of OV329 higher dosing to potentially expand dosing optionality for future studies and indications

Results

- Demonstrated favorable safety profile at all doses, with no treatment-related serious-adverse events (SAEs)
- At 7 mg (n=11 healthy volunteers across SAD/MAD), there were no adverse events considered related to study drug
- In a blinded 7 mg MAD cohort (n=8) there were a total of 19 unrelated adverse events (AEs), all were mild and transient
- No evidence of ophthalmic or retinal changes across a rigorous battery of clinical and structural measures
- Favorable tolerability profile at 7 mg dose supports Phase 2 plans and a potential best-in-category profile

OV329 was well-tolerated at all doses, with no treatment-related SAEs

Summary of potentially treatment-related and treatment-emergent AEs reported

Dosage	Adverse Event	OV329	PBO	Severity	Drug Related	Outcome
2 mg MAD	Headache	n=1	n=0	Mild (grade 1)	Possibly related (x2)	Recovered or resolved (x2)
	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	None	N/A	N/A	N/A

New

N= number of participants
(x "number") = number of events

No ophthalmic or retinal changes at all doses, including 7 mg

Ophthalmic metric*	Result
Best corrected visual acuity	No treatment-related effects
Fundus photography	No treatment-related effects
Indirect dilated ophthalmoscopy	No treatment-related effects
Automated threshold visual field perimetry	No treatment-related effects
Optical coherence tomography	No treatment-related effects

- Results consistent with prior clinical and preclinical ophthalmic safety characterization evidence demonstrating OV329 does not accumulate in the eye or change human visual health or structure
- Vigabatrin was shown to preferentially partition and accumulate in the retina, thus new 7 mg safety data supports differentiation of OV329 and potential best-in-class profile

OV329 achieves target exposures for pharmacology strategy & potential anti-convulsant activity

Dose modeling: Leveraged multiple streams of evidence

- OV329 human cortical inhibition & plasma exposure data (healthy volunteers)
- Mesial temporal lobe epilepsy repeat dosing models (mice)
- GABA-AT enzyme inhibition studies (mice)
- Vigabatrin pharmacology from therapeutic doses*

Strategy

Target enzyme inhibition for adults with focal onset seizures: ~ 50 – 60%

Modeled drug exposure in plasma to achieve anti-convulsant effect:

- ~60 ng* hr/mL – 120 ng* hr/mL

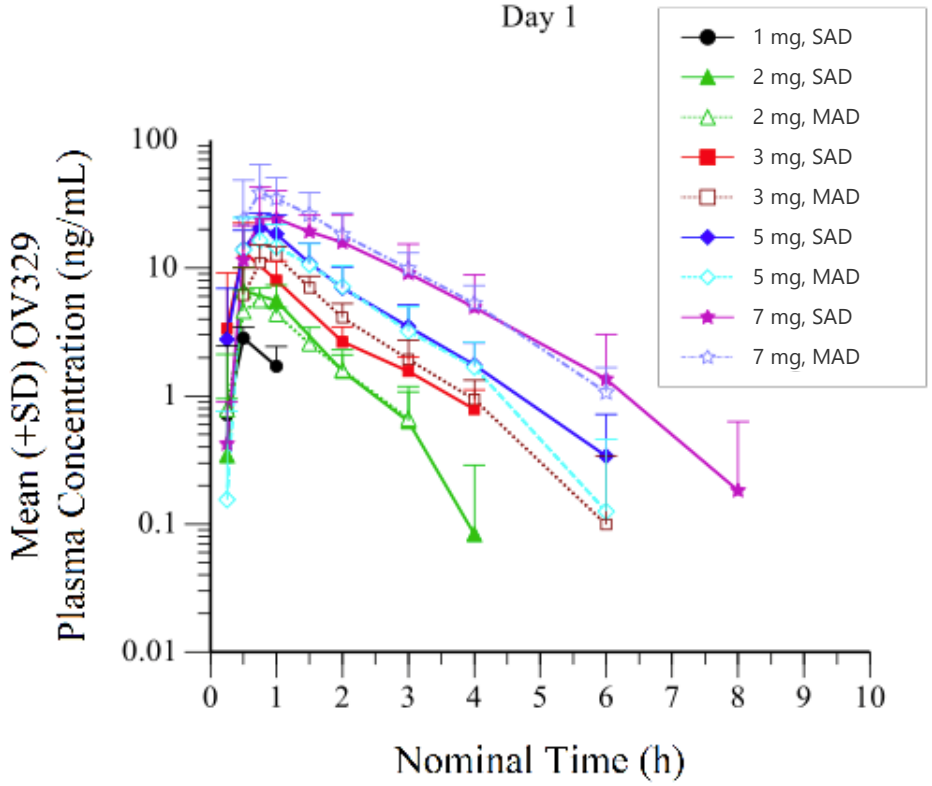
Human drug plasma exposure by dose

Dose	Demonstrated mean exposure
3 mg	52.1 ng* hr/mL
5 mg	81.7 ng* hr/mL
7 mg	154 ng* hr/mL

* Adjusted for molecular weight and potency

7 mg results reaffirmed predictable pharmacokinetic profile aligned with pharmacology strategy

- Dose dependent linear increases in AUC and Cmax demonstrated in repeat dosing
- Consistent renal clearance after single and repeated dosing
- Steady state achieved by Day 3
- Time to peak drug concentration (Tmax) is 1 hour
- OV329's potency and irreversible binding exploit the slow turnover of GABA-AT enzyme in the brain
    - Effect: Enduring enzyme inhibition and rapid half-life

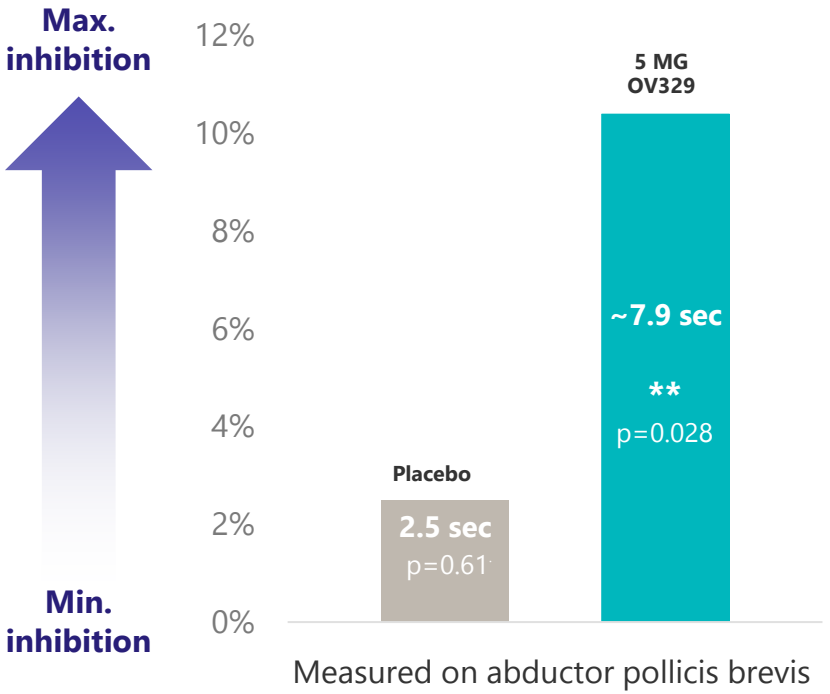


Ovid data on file

OV329 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

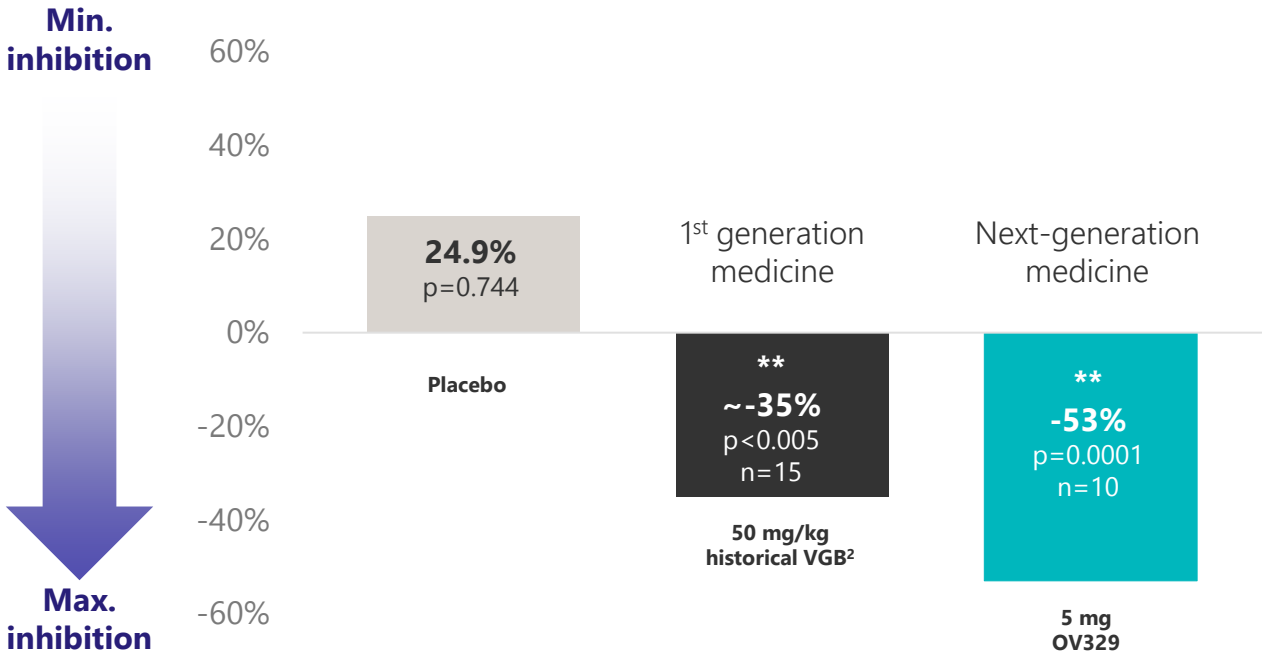


Measured on abductor pollicis brevis

Significantly increased cortical inhibition exceeding vigabatrin's 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

1. Baseline is at Day 1 prior to any treatment
2. Pierantozzi et al., Brain Res. 2004 Nov 26; 1028(1):1-8

Advancing OV329 into a Phase 2 trial & open-label study

- Strong safety profile with few treatment-related adverse events; no ophthalmic safety findings
- Demonstrated, competitive cortical inhibition as measured by multiple well recognized biomarkers
- Inhibitory effects match or exceed therapeutic doses of vigabatrin
  - Historically VGB has shown 50% or greater reduction in FOS frequency and potential for seizure freedom[1]
- Favorable tolerability profile with no adverse events associated as drug related at 7 mg dose
- 5 mg and 7 mg doses achieve drug exposure in plasma predicted to be anti-convulsant
- Current doses anticipated to optimize responder rate

1. FDA Medical Review(s) for Sabril (vigabatrin). (2009). U.S. Food and Drug Administration. [accessdata.fda.gov]

Next steps in FOS: Phase 2 PoC studies

Two, parallel PoC studies to confirm anti-convulsant activity and effect size

Open label seizure PoC study

Objective

Characterize suppression of photo-paroxysmal EEG response (PPR), which is correlated with ASM seizure reduction efficacy

Population

Patients with photosensitive epilepsy

Utility

- Demonstrates PoC in a seizure population; and potentially dose responsiveness
- Potential to deliver a milestone with possible readout results in Q4 2026

Phase 2 – Randomized placebo controlled

Objective

Characterize seizure reduction efficacy, responder rate, safety, tolerability, pharmacokinetics and clinical global impression (CGI)

Population

Adults with treatment-resistant epilepsy

Utility

- Understand anti-convulsant profile
- Reinforce indication sequencing
- Builds controlled safety database
- Informs powering and effect size insights for pivotal trials

The OV329 opportunity:
A universal mechanism for treatment resistant seizures

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Unmet need in infantile spasms

Rare, seizure manifestation in the infantile brain

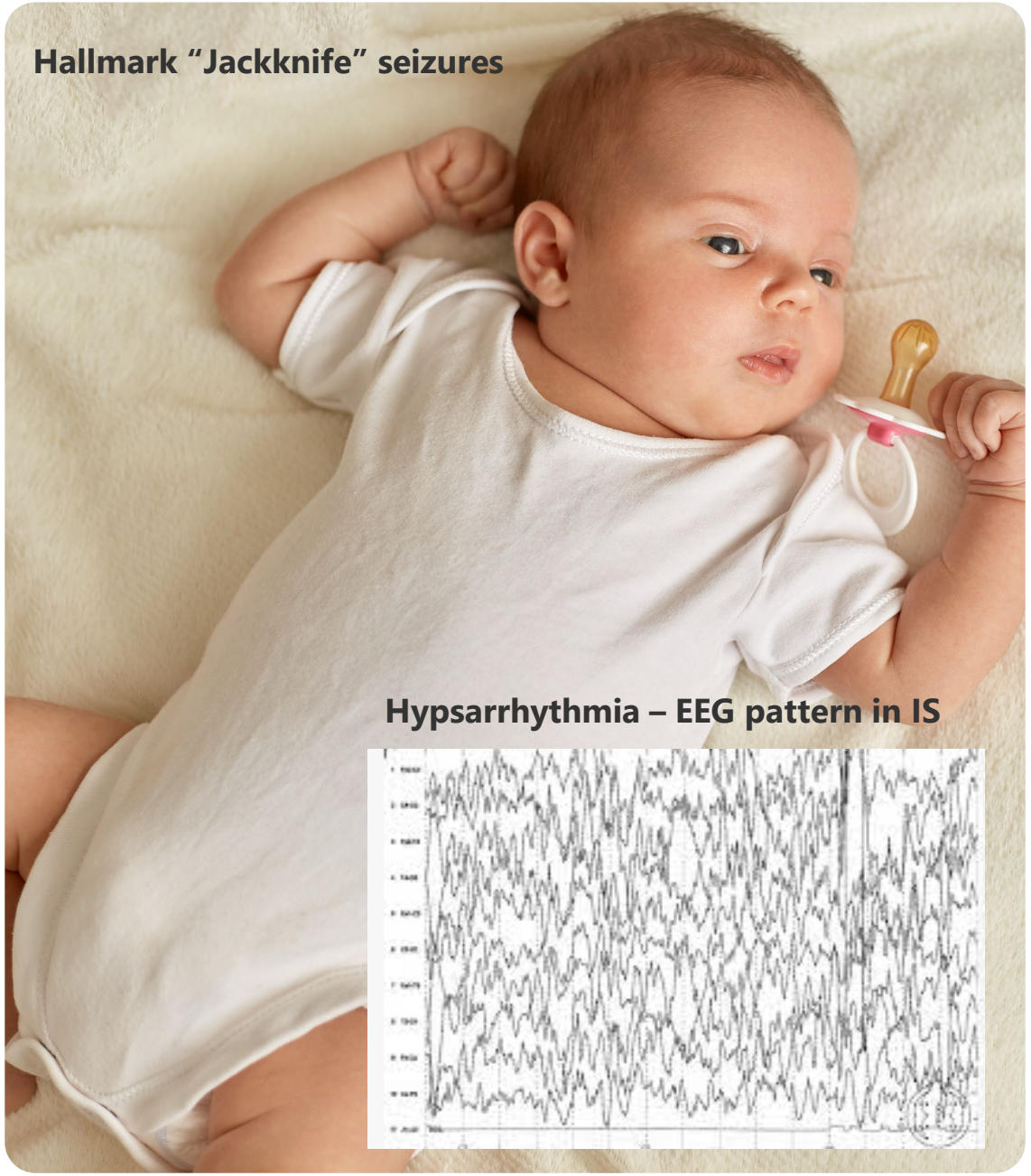
- Hallmark jackknife seizures typically occur between 4-7 months of age
- Moderate-to-severe developmental disability
- Increased mortality
- Seizures evolve to Lennox-Gastaut syndrome (LGS) or other drug-resistant seizures
- <5% have a good developmental prognosis

Treatment goal

- Early seizure control
- Improved developmental outcomes
- Mitigate development of LGS

Current standard of care

- Acthar hormone actor gel (or high dose steroids)
- Vigabatrin, includes risk of blindness



Unmet need in tuberous sclerosis complex[1]

A rare autosomal-dominant disorder of TSC1 and/or TSC2 genes

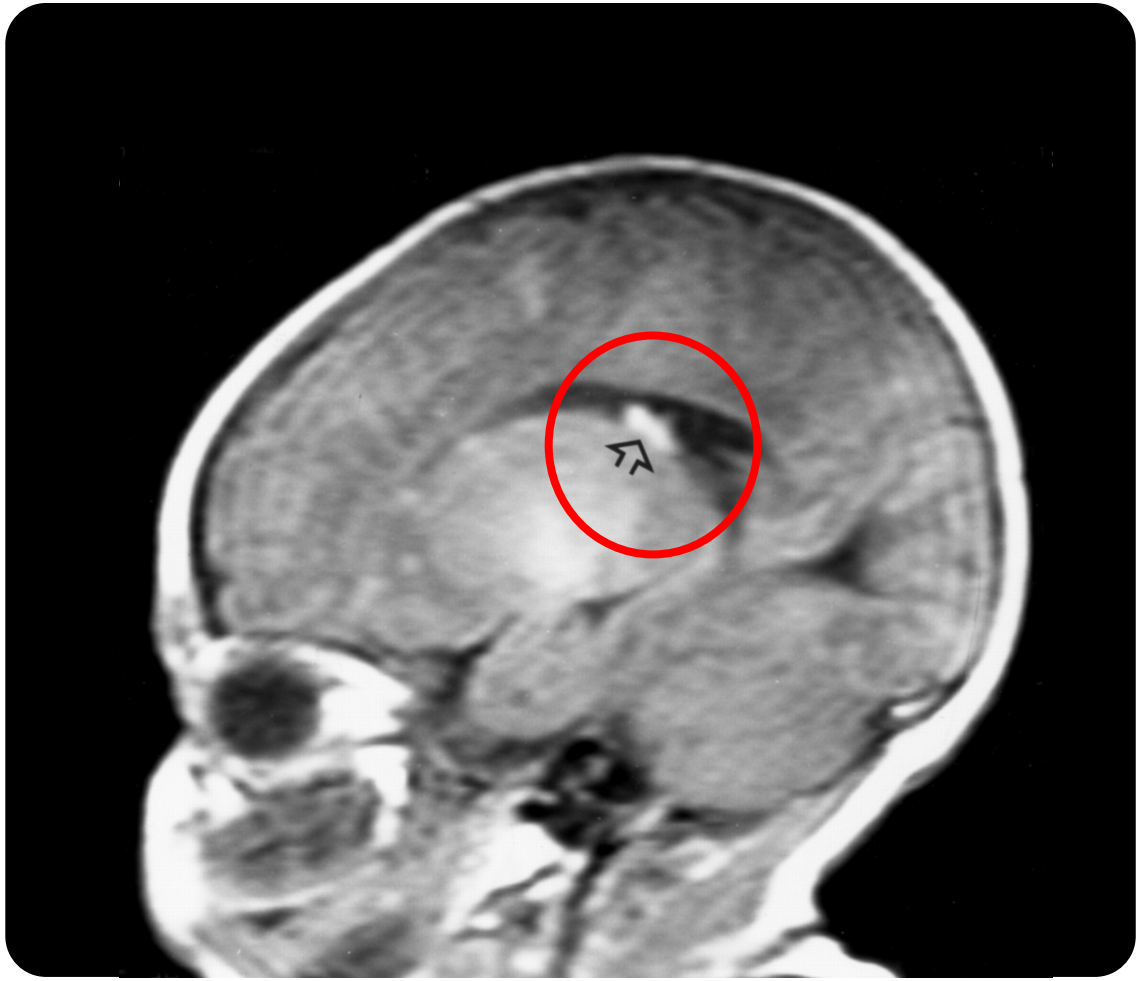
- Upregulation of the rapamycin (mTOR) pathway with subsequent excessive cell growth and proliferation
- Benign hamartomas in multiple organ systems, most frequently in brain, skin, kidneys, lungs, heart, and eyes
- Epilepsies, including focal seizures, and intellectual disability, and autism

Treatment goal

- Approximately 80% of TSC community experiences seizures
- Mitigate the developmental and neurodevelopmental outcomes

Current standard of care

- Afinitor
- Sabril



1. Northrup H, Koenig MK, Pearson DA, et al. Tuberous Sclerosis Complex. 1999 Jul 13 [Updated 2024 Aug 1].

Potential for OV329

Profile

Safety

- Therapeutic index
- Positive ophthalmic safety record
- No intramyelinic edema

Tolerability

- No anticipated sedation
- Clean profile at high dose (7mg) in adults

OV329

Potential efficacy*

- >40% freedom from infantile spasms (after 25 weeks)
- Responders >90% improvement; 46% seizure freedom

Flexibility of use

- No anticipated titration
- No DDIs

Potential to increase use if approved

Infantile spasms

- 1st line use with Acthar Gel
- Prolonged use to mitigate LGS

Tuberous sclerosis complex

- 1st line for seizure reduction
- Prevention of epilepsy from TSC (later expansion indication)

*Extrapolated from vigabatrin historical data

SABRIL (vigabatrin) sales under-reflect the sizeable market opportunity

Tuberous sclerosis complex (Addressable population 2026: U.S. = ~21K and EU5 = 20K)

	Acthar GEL (repository corticotropin injection) 80 U/mL	AFINITOR (everolimus) Tablets	Epidiolex (cannabidiol)	Sabril
Pricing	$90K[1] avg treatment course	$5 - $20K / year	~$20K/year[2]	**~$130K / year**
Average treatment duration	Two courses	Annually	Annually	**9 mos.**
Use	2nd line	2nd line	2nd line	**Limited due to visual safety**

Infantile spasms (Addressable population 2026: U.S.=4.5K and EU5=9.4K)

	Acthar GEL (repository corticotropin injection) 80 U/mL	Synthetic steroids	Sabril
Pricing	$90K[1] avg treatment course	$90 - $450/course	**$84 – 126** ($14K / mo) [2]
Average treatment duration	Two courses	A few courses	**6 – 9 mos.**
Use	1st line w/steroids	1st line	**2nd line**

Sabril

- $320M peak U.S. sales (2018)[3]
- Limited use
- Approved for infantile spasms in U.S.

1. As priced in U.S., assumes two courses of treatment at $45K per vial
2. Estimate; actual pricing is based on weight-based dosing
3. IQVIA

GABA-AT is a proven mechanism in TSC & IS

Sabril

Proven efficacy

Infantile spasms

- Freedom from spasms ~47%
- Freedom from treatment failure ~37%

TSC seizures

- Responders >90% seizure reduction
- 46% seizure freedom

Short treatment duration

- 2nd or 3rd line
- Short duration due to safety

Copious dosing

- Starting dose: 2,000 mg – 3,000 mg

Onerous monitoring

- On label - risk of irreversible blindness
- REMS with visual perimetry & ERG every 3 months

Priced for a broad population

- $14K per/mo list price
- Priced prior to post-market safety findings which limited use to acute populations

Vigabatrin historical data

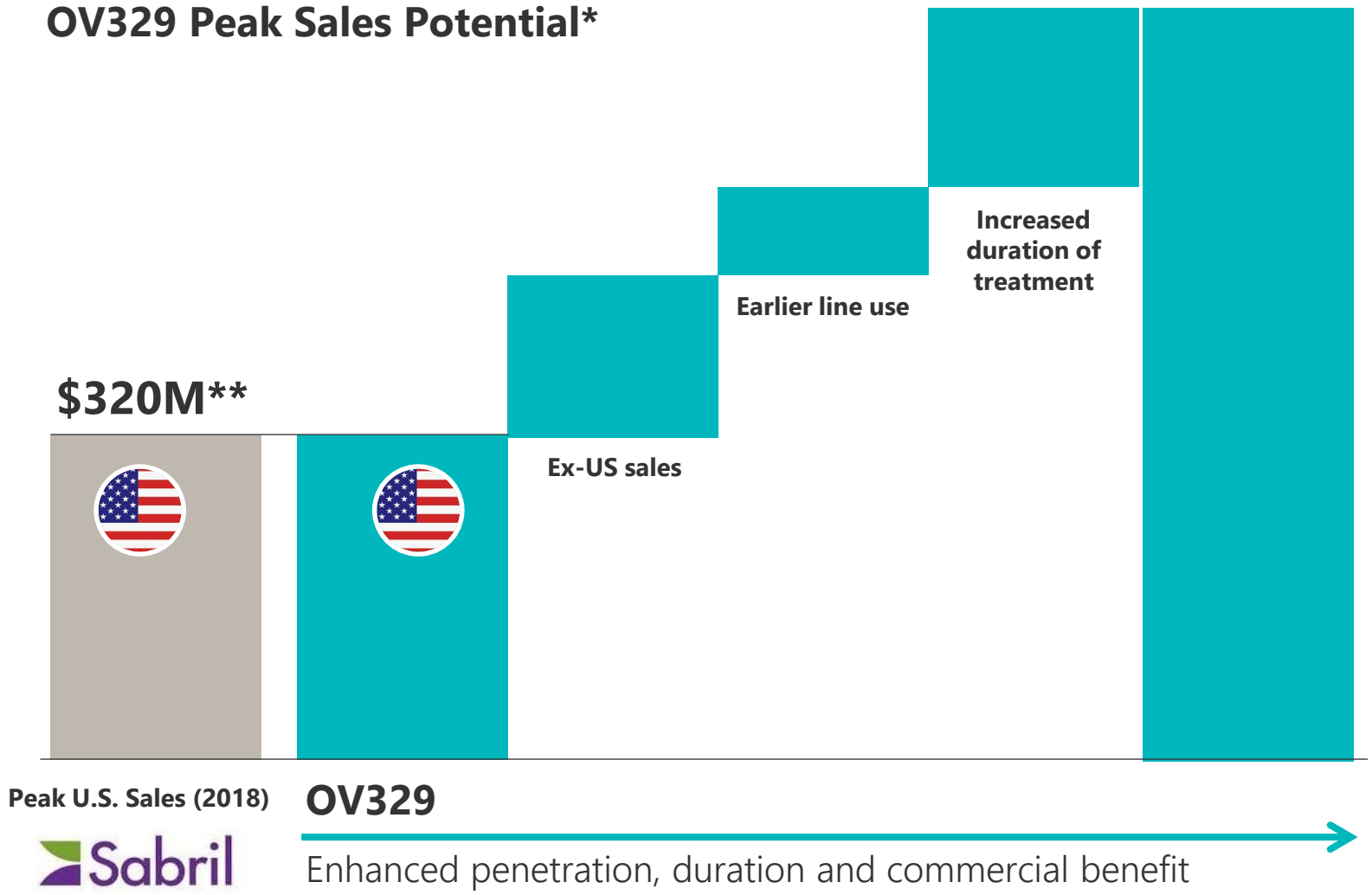
OV329 holds significant potential in TSC & IS

Anticipate earlier-line use, longer treatment duration

Validated MoA with an improved profile:
Enhanced safety, efficacy and tolerability

Differentiated pediatric formulation & weight-based pricing

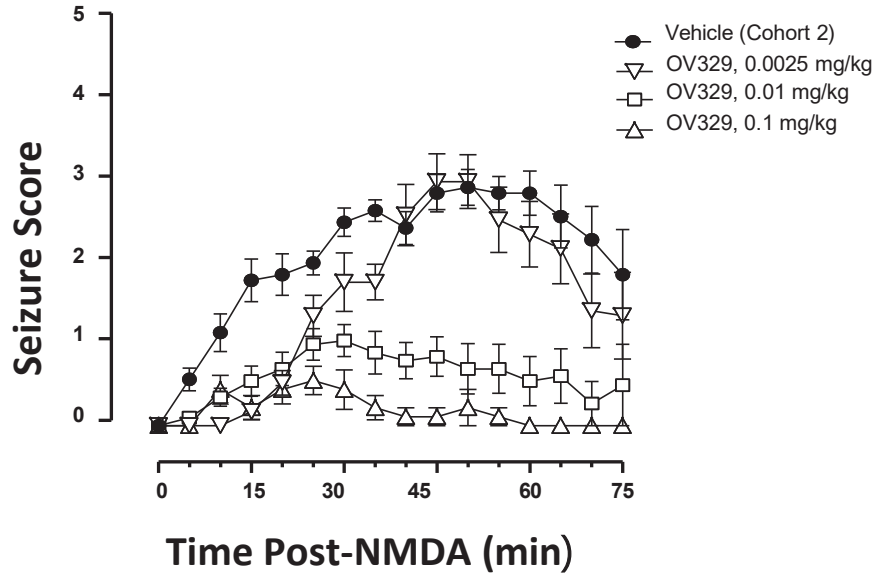
Potential for disease modification



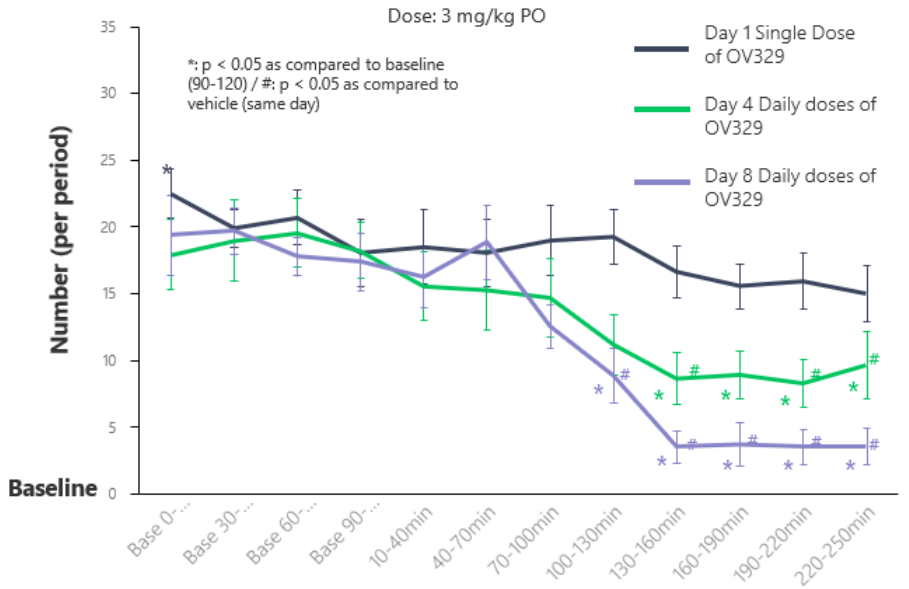
* Projected estimates
**IQVIA

OV329 shows compelling anti-convulsant 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

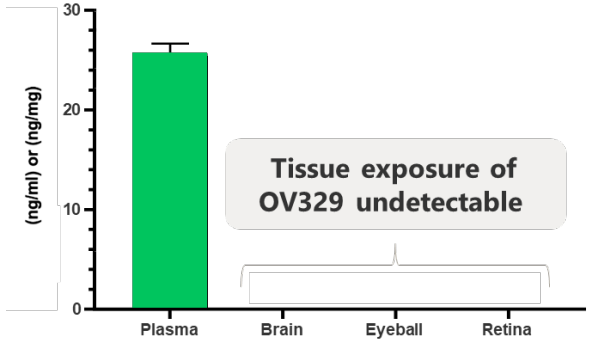
1. Ovid data on file
2. Mukherjee, J., et al. (2022). OV329, a Next-Generation GABA-AT Inhibitor, Suppresses Hippocampal Paroxysmal Discharges Following Repeat Dosing in a Mouse Model of Mesial Temporal Lobe Epilepsy. Poster presented at the American Epilepsy Society 2022.

OV329 does not accumulate in the retina like vigabatrin (VGB)

No accumulation Of OV329 detected in the eye or retina, vigabatrin accumulates[1,2]

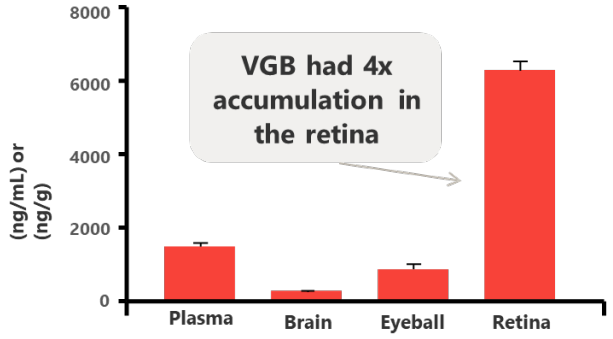
OV329

Mean Plasma and Tissue Concentration 5.0 mg/kg/day

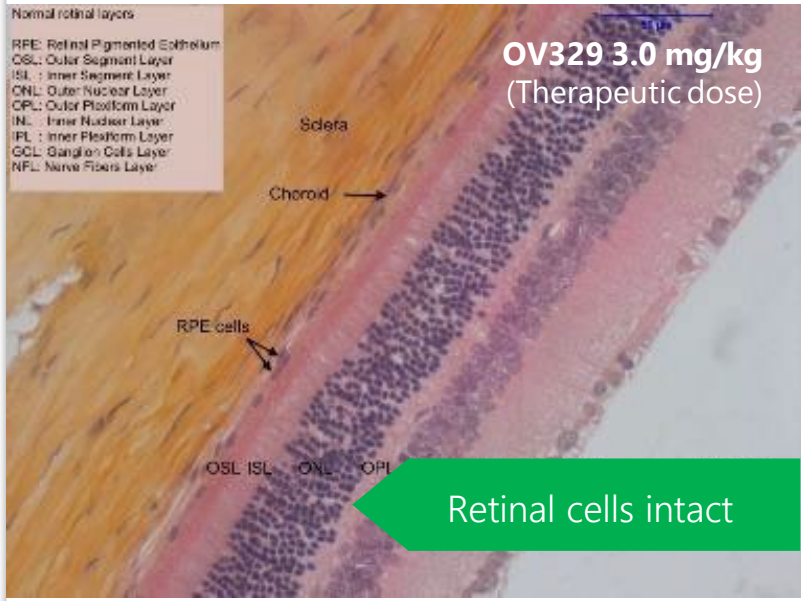


VIGABATRIN

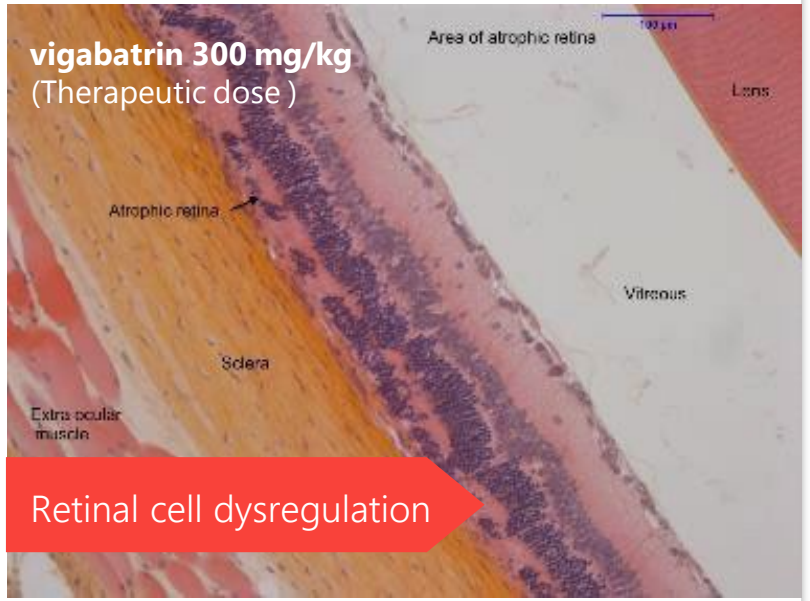
Mean Plasma and Tissue Concentration at 80.0 mg/kg/day



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



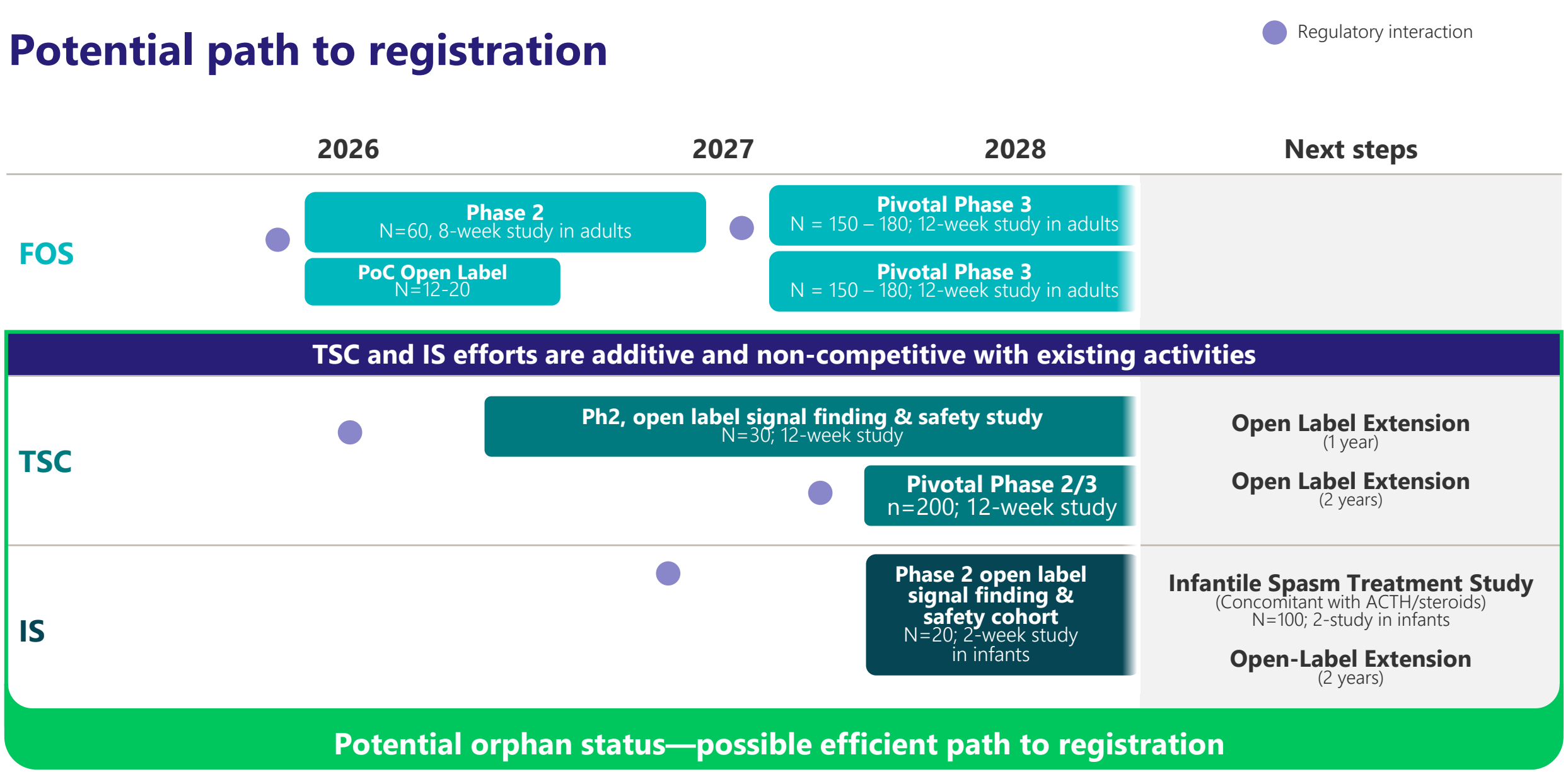
Ocular changes in more than half of rats treated (300 mg/kg)

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

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)

Ovid data on file

Potential path to registration



Development paths are not mutually exclusive and are dependent on global regulatory feedback

A potential win for patients, shareholders and Ovid

- **Additive expansion programs in de-risked indications; running parallel with FOS programs**
- **Compelling orphan commercial market in population with high need & few treatments**
- **Increases Ovid's mid-term PoC milestones and catalyst cadence**
- **Differentiated adult & pediatric (weight based) formulations; separate IP & commercial considerations**
- **Potential accelerated path to registration with pivotal Phase 2/3 and orphan designation[1]**
- **Potential to enhance OV329 and Ovid value**

1. Pending regulatory feedback; may have to conduct Ph 2 followed by Ph 3.

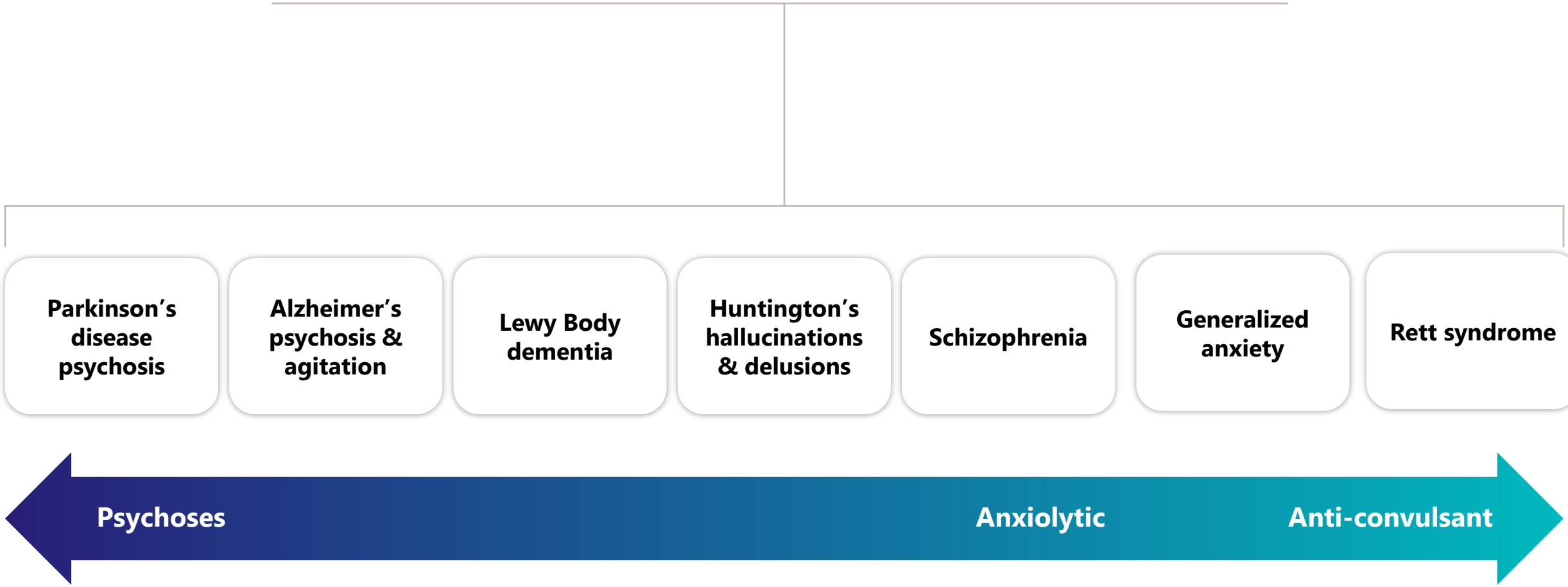
OV4071, a potential first-in-class, direct activator of KCC2 for chronic conditions

NEW UPDATES

OV4071, cleared for Phase 1 clinical trial

- Potential first-in-class oral KCC2 direct activator, OV4071, cleared for Phase 1 studies
- On-track to initiate Phase 1 in Australia
- Intend to initiate proof-of-mechanism ketamine study in H2 2026
- Proof-of-concept patient studies to begin in late 2026/early 2027
- Established safety of drugging target and potential signal with KCC2 tool program
- **Hosting KCC2 R&D Day on April 14, 2026**

Opportunity:
OV4071 has broad syndromic psychoses applications



KCC2 normalizes inhibitory/excitatory balance in neurons and maintains GABA's inhibitory tone[1]

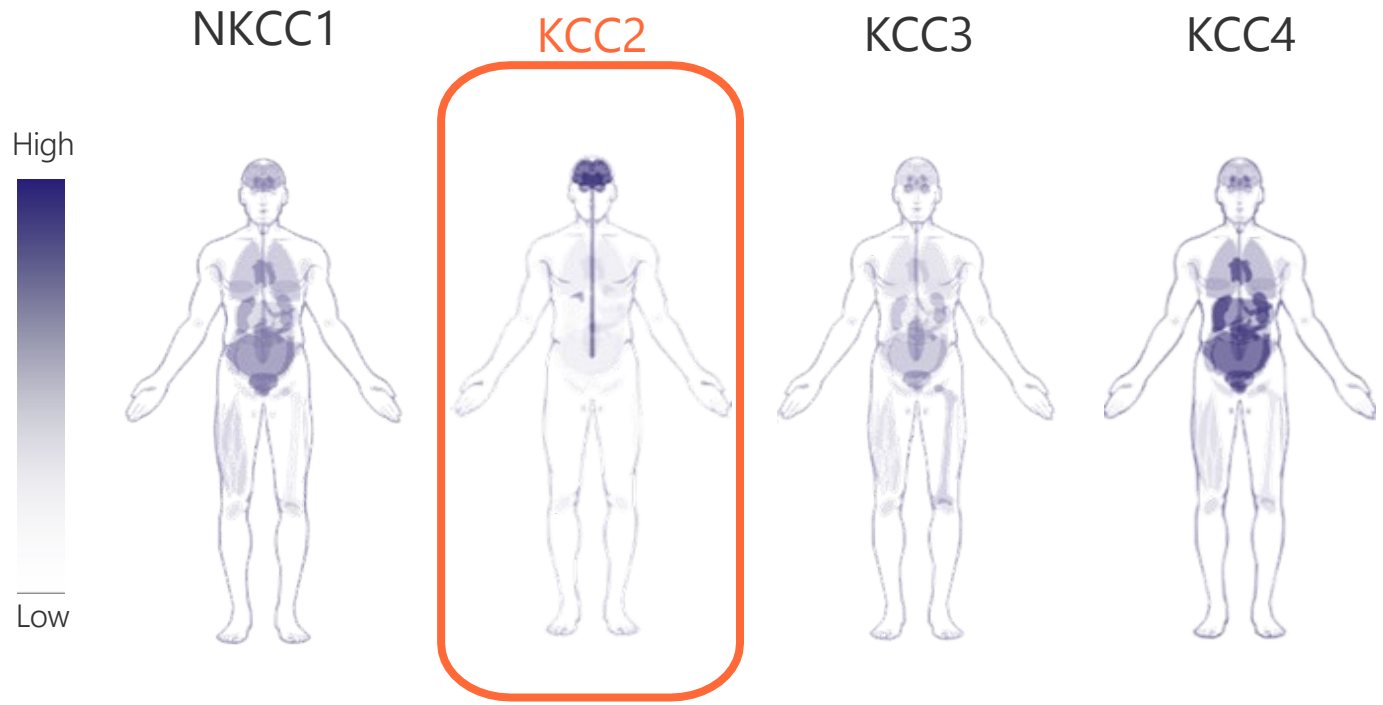
"Master switch" for neurological disorders

Where hyperexcitability is core to pathophysiology

Safety inherent in target

- Unlike enzymes, KCC2 cannot push beyond electrochemical equilibrium
- Driven by electrochemical gradients (K^+ and Cl^-)
- Self-limiting activation is intrinsic to KCC2 and supports safety in chronic use

KCC2 protein expression is confined to the CNS



KCC2 is an isoform of the potassium–chloride cotransporter family, specifically the neuron-specific member encoded by SLC12A5

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

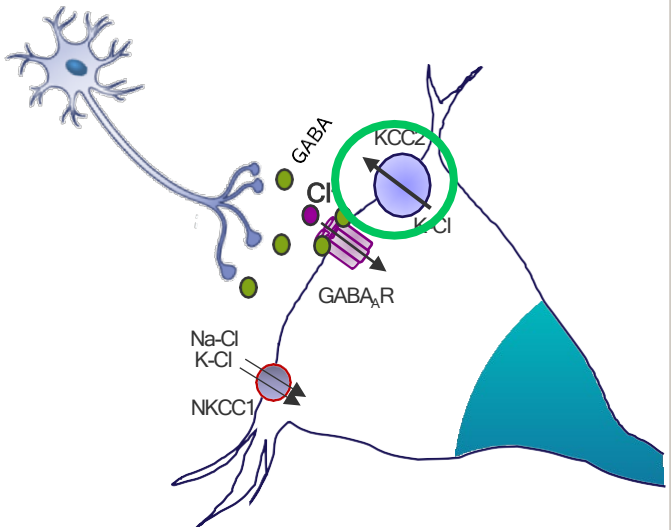
Regulates chloride gradient

Manages the passive inward entry of Cl^- through activated GABA channels

Maintaining low intracellular chloride is critical for hyperpolarization

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

Healthy Neuron



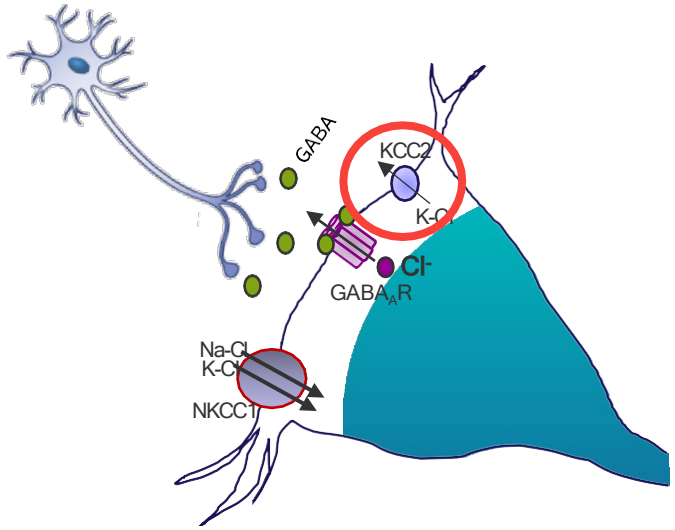
GABA → **inhibitory**

Intracellular chloride

Healthy ↑KCC2

'blanket of inhibition' in brain

Pathological Conditions



GABA → **excitatory**

Intracellular chloride

Pathology ↓KCC2

hyperexcitable circuitry

1. Pressey et al. "Chloride transporters controlling neuronal excitability", https://doi.org/10.1152/physrev.00025.2021
2. 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

OV4071 overview

Pharmacology

- Orally available
- Highly potent: 20x potency over OV350
- 60x half-maximal effective concentration (EC50) reached in repeat dosing
- Consistent plasma exposure
- Highly efficient CNS penetration: brain:plasma > 1:1
- No sedation observed

Pharmacodynamics

- Profile comparable to atypical antipsychotic in phenotypic screens
- Strong effect in hyperlocomotion-induced psychoses models, with comparable activity to marketed agents
- Rescued cognition in Methyl-CpG binding protein 2 (MeCP2) model of Rett syndrome
- Activity in iPTZ seizure model (in combination with diazepam)
- Motor function improvement in Huntington's disease model
- Neuropathic pain and grip strength improvement

IND-enabling studies (complete)

- Rat and dog Good Laboratory Practice (GLP) complete; estimated safety margins 15 – 17-fold

Clinical Plans

- Phase 1 HV study - Q2 2026
- Biomarker "challenge" studies – mid-2026
- Proof of Concept (PoC) studies in Parkinson's Disease Psychosis (PDP) and Lewy Body Dementia (LBDP)
- Potential schizophrenia PoC Phase 2 study

NEW UPDATES

KCC2 portfolio

Established class safety & potential signal in humans

(Tool program findings reported Dec. 2025)

25+ **proof of mechanism and PD studies validating activity in:**

- Psychoses
- Seizures
- Rett
- Anxiety
- Huntington's
- Neuropathic pain

Binding site established; direct activation confirmed

Initiating OV4071 first-in-human study (FIH) in Q2 2026

- Potent, pharmacodynamic (PD) activity at low doses
- **15 – 17x** safety margins
- Manufacturing complete

Robust, productive discovery engine

Next-generation chemistry & novel IP

2 next-generation development candidates +

7 additional neuroactive molecules

The potential of KCC2 direct activation

A fulcrum in neural excitation/inhibition; fundamental biological target

Highly selective, precision small molecules

Expansive therapeutic applicability

Preferable tolerability & safety (no sedation)

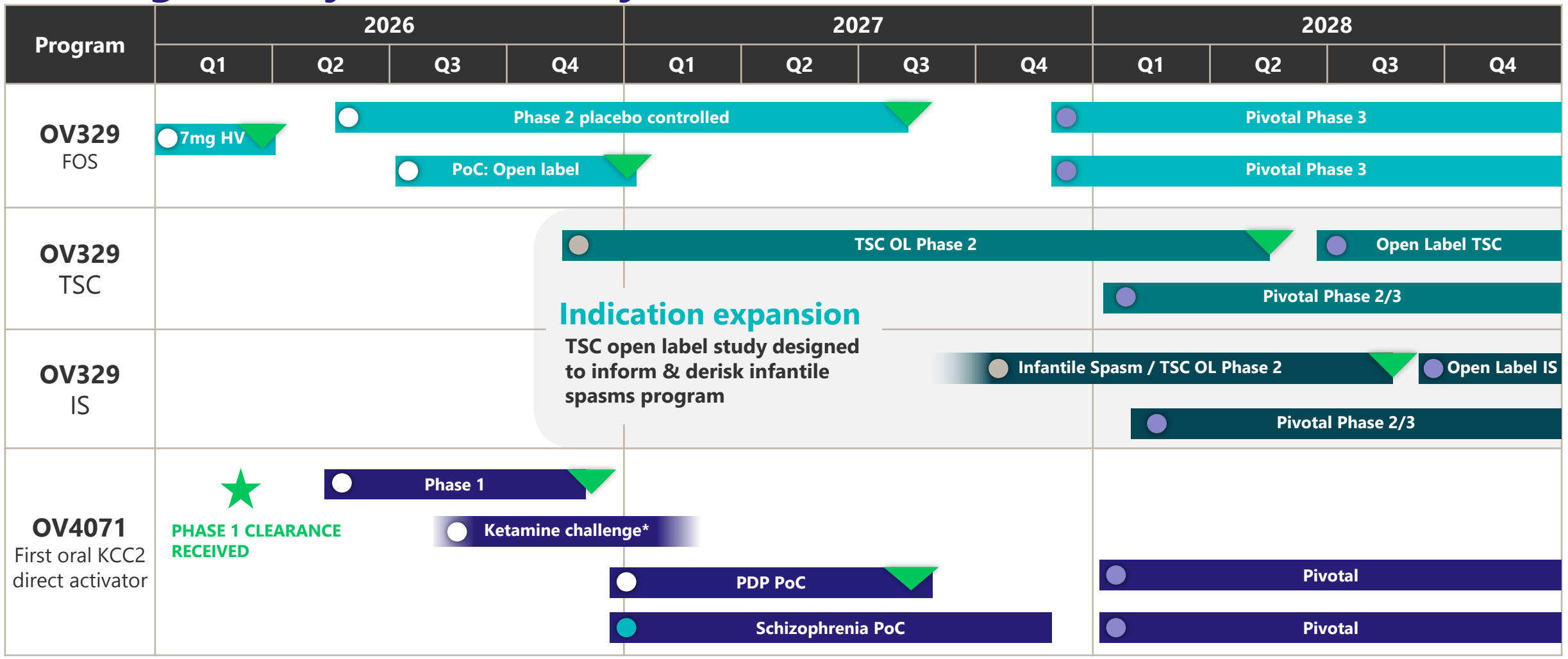
Potential for oral, injectable and IV administration

Only confirmed direct activators

Replenishing portfolio of unique molecules to fuel a CNS franchise in disorders with great unmet need

Plan potentially unlocks OV329 full value creating a catalyst rich runway

- Funded by Ovid runway
- Pivotal and OLE trials that would require funding post PoC
- Indication expansion with financing
- Funded assuming full exercise of warrants



Cash runway into 2029 fueling multiple potential catalysts**

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

Ovid Therapeutics

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