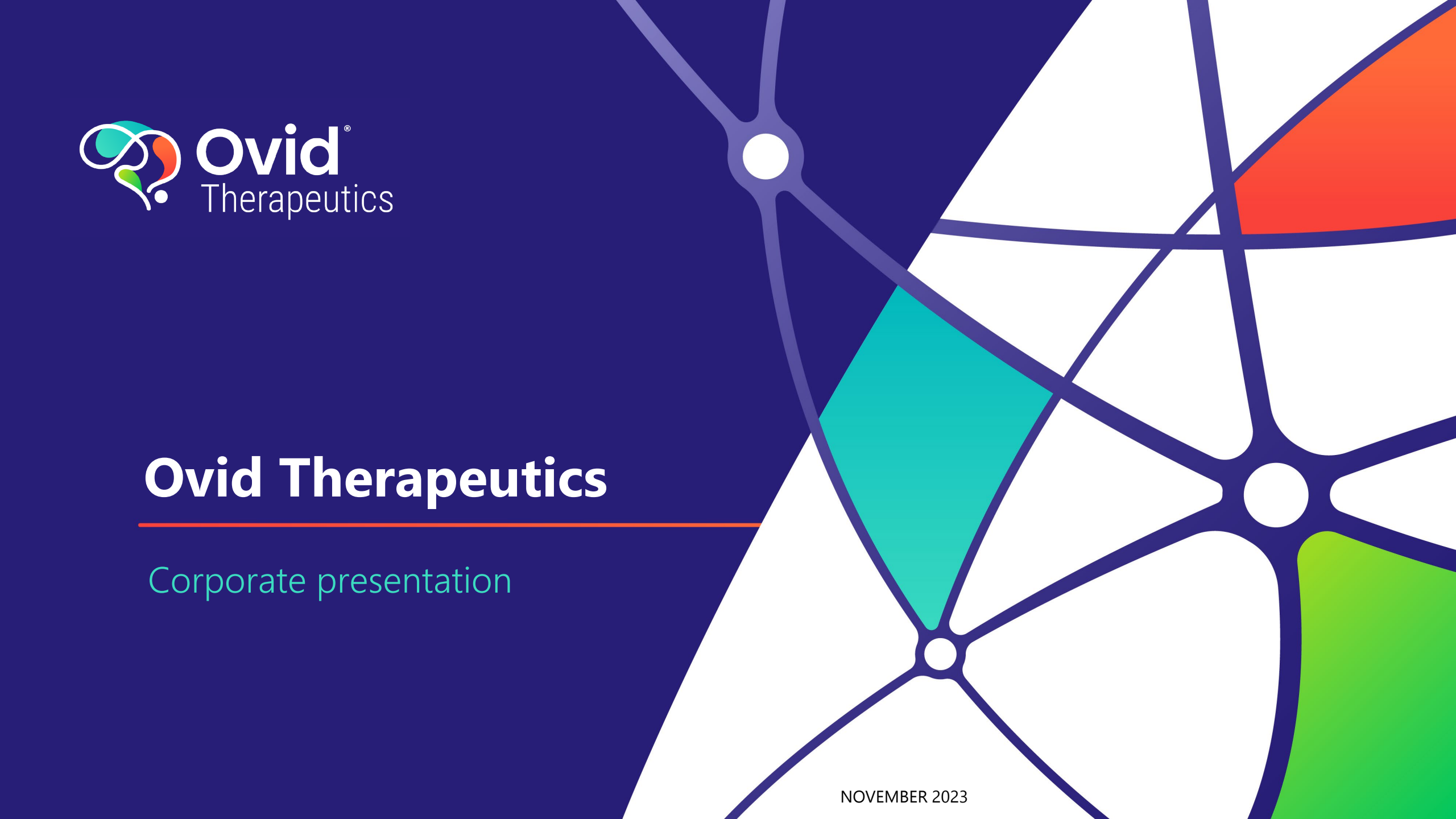


Ovid Therapeutics

Corporate presentation

NOVEMBER 2023

Forward looking statement

This presentation contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995 including, without limitation, statements regarding the timing and development of Ovid's product candidate pipeline and achievement of expected near- and long-term milestones; the potential therapeutic benefits of Ovid's current or future product candidates and pipeline programs; the reporting of data for the potential Phase 1 study in healthy volunteers for OV329; the potential use of OV329 to treat rare and treatment-resistant forms of epilepsy and seizures; the clinical and regulatory development of OV329, including the anticipated timing of clinical trials of OV329; the likelihood that data for OV329 will support future development and therapeutic potential; the potential development of OV350 and other KCC2 compounds in the Company's library; the potential timing of a potential IND filings for OV329 and OV350; the suitability of the Company's library of novel, direct KCC2 transporter activators for a range of formulations and administrations that would make it possible to pursue both chronic and acute epilepsies; the potential development and therapeutic opportunity of OV888 (GV101) and other Rho/Rho associated coiled-coil containing protein kinase 2 inhibitors; and the potential safety, selectivity and potency of OV888 (GV101) and other ROCK2 inhibitors; the potential use of OV888 (GV101) and other ROCK2 inhibitors to treat cavernous cerebral malformations and other rare central nervous system disorders; the potential timing of the pivotal formulation for OV888 (GV101); the potential timing of clinical studies for OV888 (GV101) and the resulting data; the timing for the completion of Takeda's two pivotal Phase 3 trials evaluating soticlestat for Lennox-Gastaut and Dravet syndromes; the potential timing of regulatory decisions on soticlestat; the success of Takeda's trials in soticlestat; the duration of the Company's cash runway, and the expectation that it will support the advancement of the Company's pipeline; Ovid's business development intentions; the success of any licensing or partnering opportunities; the success, timing, ability to attract and maintain strategic collaborations; the clinical and regulatory development and potential commercialization of soticlestat, OV329, OV350, OV888 (GV101) or any of Ovid's other current or future product candidates and pipeline programs and market opportunities. You can identify forward-looking statements because they contain words such as "will," "may," "plan," "believes," intends," "anticipates," "design," "advance," "target," "seek," "expects," "demonstrates," "observe," and "potential," and similar expressions (as well as other words or expressions referencing future events, conditions or circumstances).

Forward-looking statements are based on Ovid's current expectations and assumptions. Because forward-looking statements relate to the future, they are subject to inherent uncertainties, risks and changes in circumstances that may differ materially from those contemplated by the forward-looking statements, which are neither statements of historical 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, risks related to Ovid's ability to achieve its financial objectives, the risk that Ovid may not be able to realize the intended benefits of its technology or its business strategy, risks related to Ovid's ability to identify business development targets or strategic partners, to enter into strategic transactions on favorable terms, or to consummate and realize the benefits of any business development transactions and risks to Ovid's or any of its partners' abilities to meet anticipated deadlines and milestones. Additional risks that could cause actual results to differ materially from those in the forward-looking statements are set forth under the caption "Risk Factors" in Ovid's Quarterly Report of Form 10-Q filed with the Securities and Exchange Commission (SEC) on November 3, 2023, and in future filings Ovid makes with the SEC. Any forward-looking statements contained in this press release speak only as of the date hereof, and Ovid assumes no obligation to update any forward-looking statements contained herein, whether because of any new information, future events, changed circumstances or otherwise, except as otherwise required by law.

Overview

+ Strong balance sheet

$87.1M	in cash, cash equivalents and marketable securities[1]
$30.0M	in non-dilutive capital from Ligand Pharmaceuticals[2]
70.6M	shares of common stock outstanding[3]

Current cash runway expected into 2026

Potential for a non-dilutive capital stream from Takeda

+ Veteran team

with a track record of developing and commercializing blockbuster medicines

Differentiated epilepsy & seizure-related therapeutic franchise

- 3 small molecule programs (4th program sold to Takeda and we retain significant financial interest)
- Potential 1st-in-class or potential best-in-class medicines
- Novel, complementary mechanisms of action for the potential treatment of epilepsy & seizures
- Significant unmet need

5 potential upcoming pipeline events in next 12-15 months

- Complete multiple ascending dose study to evaluate a pivotal formulation for OV888 - H1 2024
- Initiate proof-of-concept trial for OV888 in cavernous malformation – H2 2024
- Surrogate biomarkers, safety and PK results for OV329 oral formulation – H2 2024
- IND for an intravenous formulation of OV329 – H2 2024
- Anticipated submission of 1st IND from KCC2 portfolio (OV350) – H2 2024

Anticipated from Takeda (Ovid's rights to soticlestat were out-licensed to Takeda)

- Data from a Phase 3 pivotal study of soticlestat in Lennox-Gastaut syndrome (SKYWAY); conducted by Takeda
- Data from a Phase 3 pivotal study of soticlestat in Dravet syndrome (SKYLINEY); conducted by Takeda
- Series of potential regional regulatory filings for soticlestat; conducted by Takeda

1 As of 9/30/23
2 Received for 13% interest of potential milestones and royalties Ovid is eligible to receive from Takeda if soticlestat is approved and commercialized
3 As of 9/30/23, on an as if converted basis

Expected to be first-in-class or best-in-class mechanisms of action

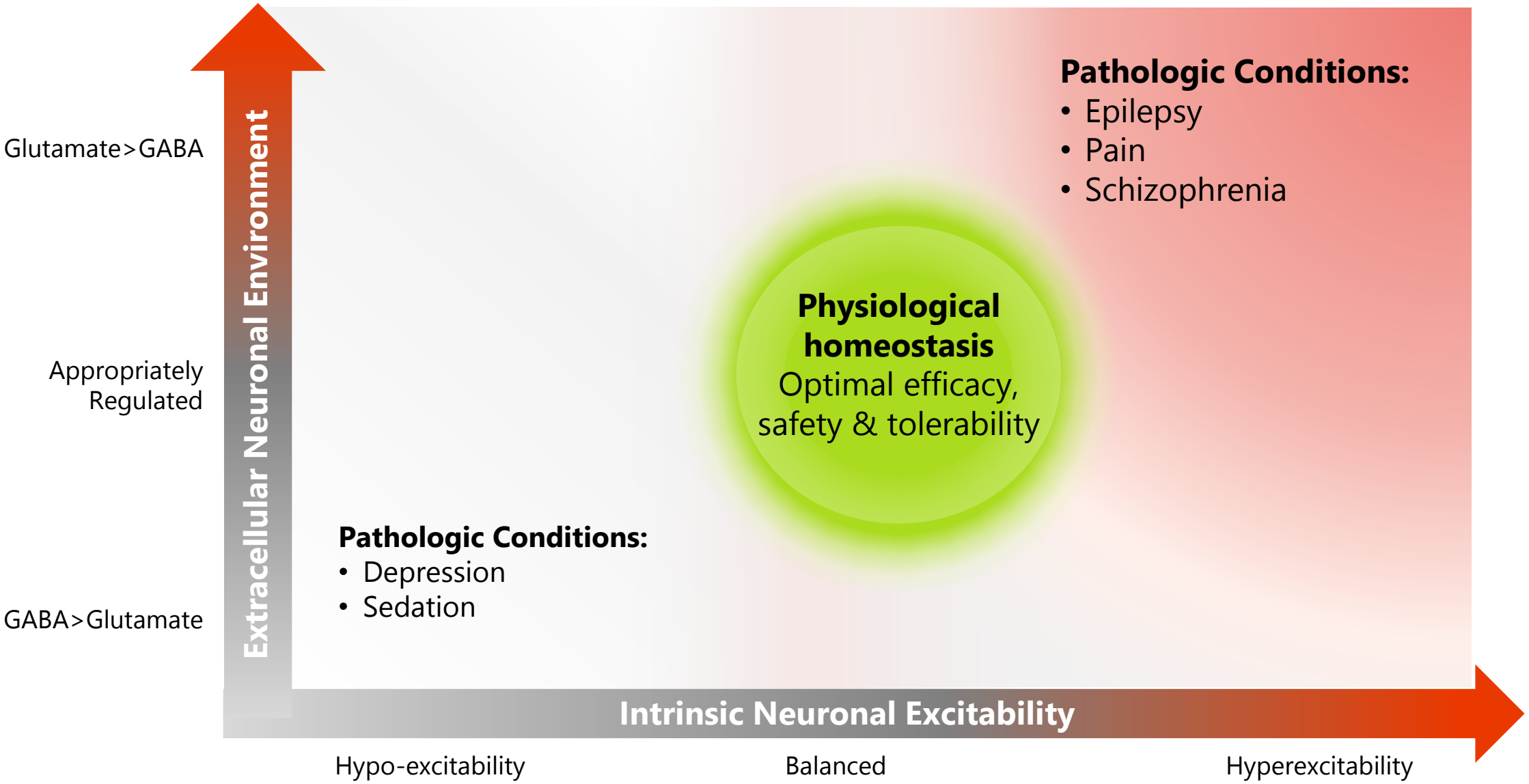
PROGRAMS	INDICATION/TARGET	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	ANTICIPATED MILESTONES
SOTICLESTAT Cholesterol 24-hydroxylase inhibitor Out-licensed to Takeda	Dravet syndrome					• Phase 3 data from 2 registrational trials • Filing marketing authorization submissions in Takeda's FY 2024
	Lennox-Gastaut syndrome					
ROCK2 PLATFORM & OV888* Selective ROCK2 inhibitor Collaboration with GRAVITON	Brainstem cavernous malformations Undisclosed rare CNS indications					• MAD completion H1 2024 • POC study initiation H2 2024
OV329 GABA-aminotransferase inhibitor In-licensed from: Northwestern University	Oral formulation for chronic epilepsies (conditions with focal seizures, tuberous sclerosis, infantile spasms)					• Phase 1 target engagement, PD marker & safety H2 2024
OV329 GABA-aminotransferase inhibitor In-licensed from Northwestern University	IV formulation for acute and chronic seizures					• IND in H2 2024
KCC2 PLATFORM & OV350 KCC2 transporter activators In-licensed from: AstraZeneca	Resistant epilepsies and other neuropathologies					• IND for OV350 in H2 2024
UNDISCLOSED ROCK2 INHIBITOR PROGRAMS						

*Graviton is conducting development of OV888 (formerly GV101) through Phase 2, which will be directed by a Joint Development Committee that includes members of both Graviton and Ovid.

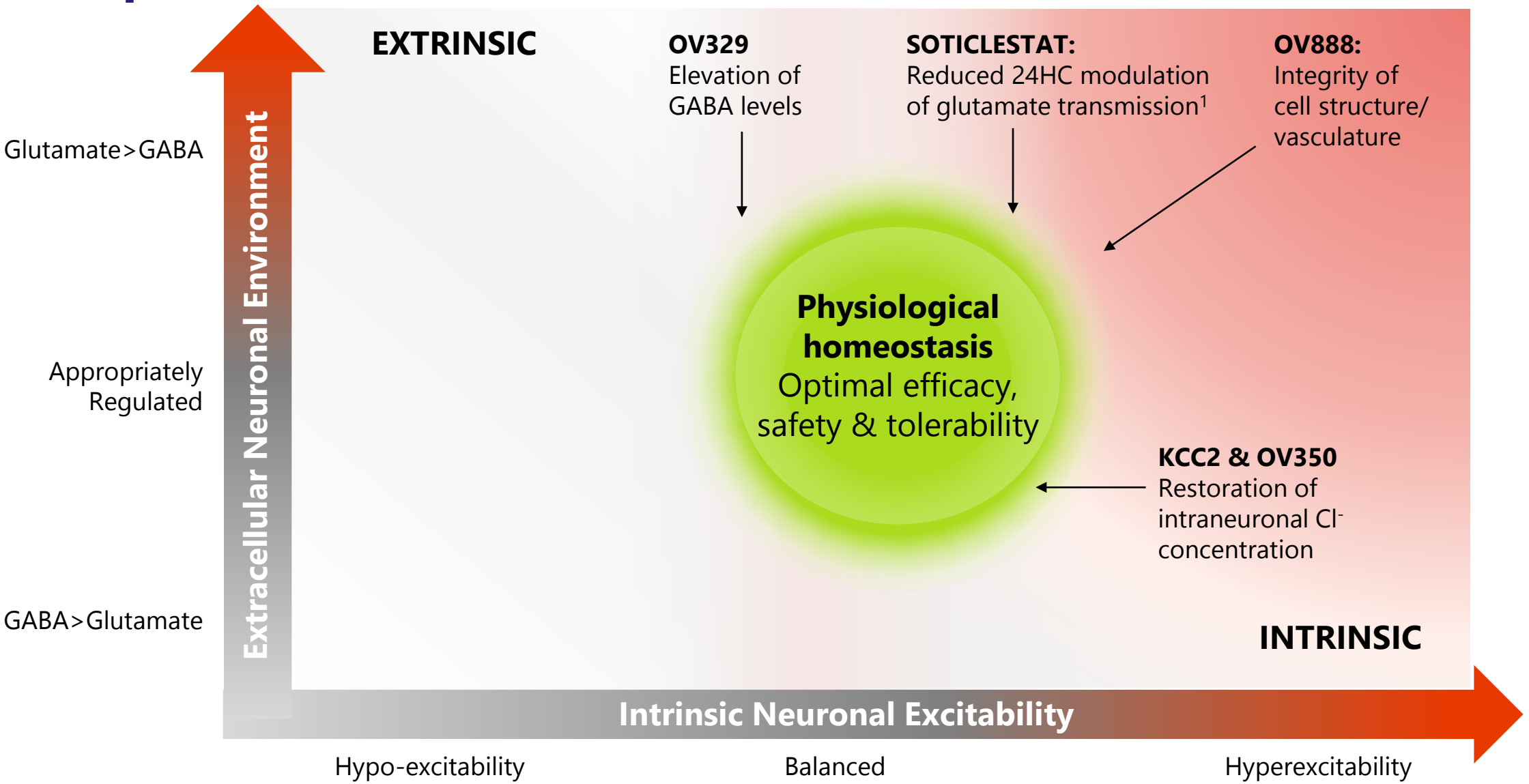
Scientific & pipeline strategy

- ✓ Exclusively targeted small molecules
- ✓ Expected to be first-in-class or best-in-class mechanisms of action
- ✓ Under-addressed biological targets expressed in CNS
- ✓ Mechanisms to modulate metabolic, enzymatic, intracellular & structural causes of hyperexcitability
- ✓ Potential application in multiple indications for which hyperexcitability is the cause for the pathology

The goal of many CNS medicines: Neuronal homeostasis (balance)



Ovid strategy:
Unique mechanisms to achieve neuronal balance (homeostasis)



1) Out-licensed rights to Takeda

Ovid mechanisms of action

Seeking to mitigate extrinsic & intrinsic causes of neuronal hyperexcitability

Metabolic & enzymatic:
Modulate extracellular neurotransmitter balance

Cholesterol 24 hydroxylase inhibition (soticlestat): Reduces glutamatergic signaling and glial cell inflammation

GABA-AT inhibition (OV329): Chronic and persistent elevation of GABA leads to profound tonic inhibitory activities in neurons

Structural & cellular integrity:
Restore endothelial cell junction integrity (ROCK2 inhibition)

ROCK2 inhibition (OV888, previously GV101): Improving endothelial integrity to reduce leakage & bleeds

Cellular intrinsic properties:
Restore chloride homeostasis in neurons

KCC2 direct activation (OV350): Restoring proper chloride homeostasis by activating the K+/Cl- co-transporter leads to rebalance of excitatory/inhibitory response of neurons

Specific mechanism references on pages 11, 20, 26, 34

Soticlestat

A first-in-class cholesterol 24 hydroxylase inhibitor for the potential treatment of Lennox-Gastaut syndrome & Dravet syndrome

Overview

UPDATE

Phase 3 global studies (ongoing)

- SKYLINE trial - Dravet syndrome
- SKYWAY trial - Lennox-Gastaut syndrome

Anticipated global regulatory filings in Takeda's FY2024

Trial completion estimates and site updates available on **www.ClinicalTrials.gov**

- First-in-class, selective inhibitor of cholesterol 24-hydroxylase
- Believed to decrease glutamatergic signaling with the potential to reduce seizure susceptibility and improve seizure control
- Studied in one of the most robust development programs for developmental and epileptic encephalopathies (DEE)
- To-date, has demonstrated sustained seizure reduction efficacy, safety & tolerability with no anticipated monitoring in clinical trials
- Planned indications:
  - Lennox-Gastaut syndrome
  - Dravet syndrome

Evidence of clinical findings included on subsequent slides.

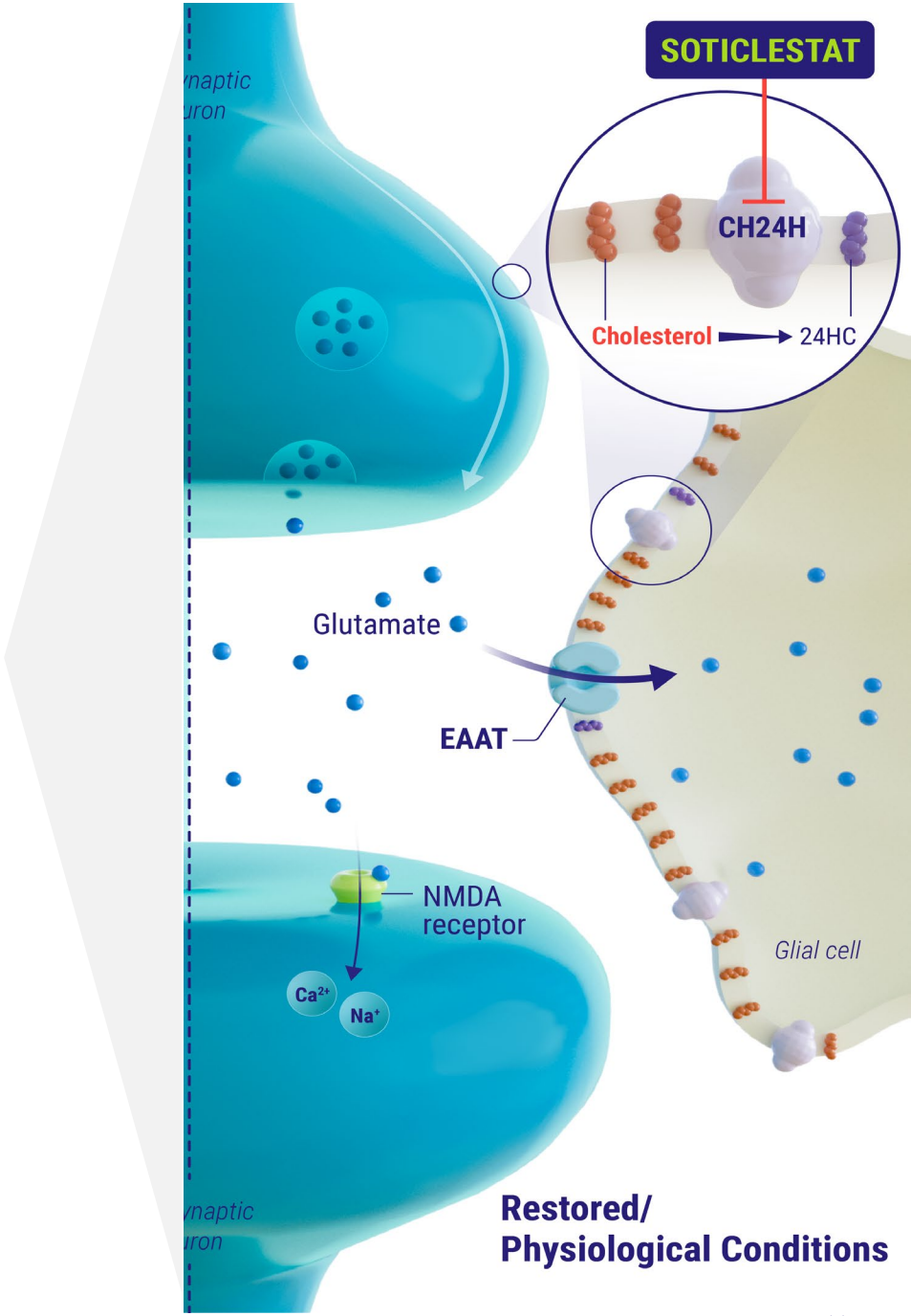
Soticlestat: Novel mechanism of action

- Preclinical findings showed:[1,2,3,4]
  - Soticlestat selectively binds to CH24H
  - Dose-dependently reduced brain 24HC levels in mice

- 24HC reduction is multi-modal & ameliorates:
  - Over-activated glutamatergic signaling
  - Inflammation

- Clinical studies in both healthy volunteers and DEE patients confirmed a dose-dependent reduction of circulating levels of 24HC in humans[5]

- Thus, reducing seizure susceptibility and improving seizure control

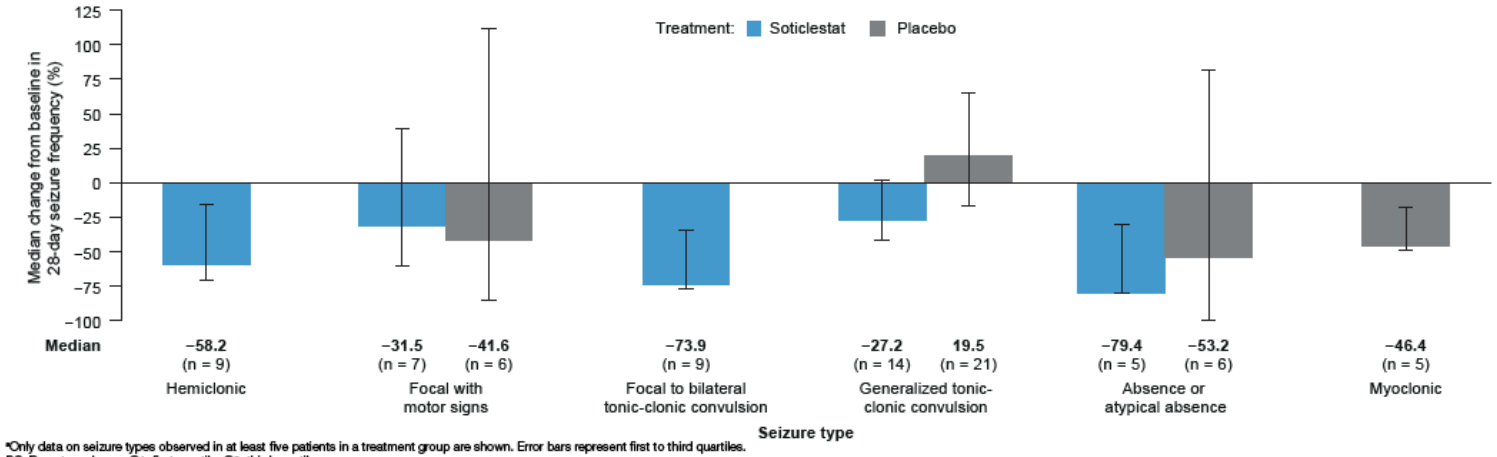


1. Nishi T, et al. Sci Rep (2020) 10: 17081
2. Salamone A, et al. Poster presented at: ECE 2018.
3. Nishi T, et al. Neurology (2018) 15 Suppl: P5.264 (Poster at: AAN 2018)
4. Sodero. A.O et al. EMBO (2012) 31: 1764-73
5. J. Halford et al. A phase 1b/2a study of soticlestat as adjunctive therapy in participants with developmental and/or epileptic encephalopathies, Epilepsy Research, Volume 174, 2021, 106646,

Phase 2 (ELEKTRA): Post hoc analysis indicates soticlestat potential in reducing frequency of multiple seizure types[1]

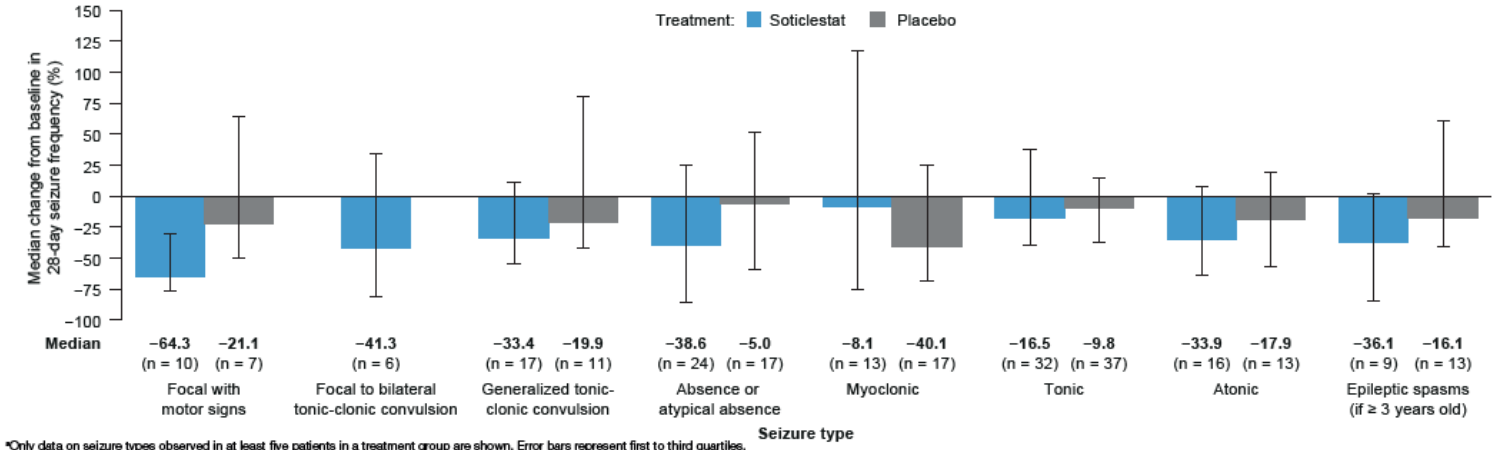
- Post hoc analysis conducted of DS & LGS patients in Phase 2, ELEKTRA study
- Soticlestat was numerically superior to placebo in all but two seizure types over the full 20-week treatment period
- Dravet patients experienced reduction in seizure frequency across:
  - Hemiclonic seizures
  - Focal to bilateral tonic-clonic seizures
  - Generalized tonic clonic seizures
  - Absence or atypical absence seizures
- LGS patients experienced a reduction in seizure frequency across:
  - Focal seizures with motor signs
  - Focal to bilateral tonic clonic seizures
  - Generalized tonic clonic seizures
  - Absence seizures
  - Atonic seizures
  - Epileptic spasms

Figure 1. Median (Q1, Q3) percentage change in seizure frequency from baseline over the full 20-week treatment period in patients with DS.[a]



[a]Only data on seizure types observed in at least five patients in a treatment group are shown. Error bars represent first to third quartiles.
DS, Dravet syndrome; Q1, first quartile; Q3, third quartile.

Figure 2. Median (Q1, Q3) percentage change in seizure frequency from baseline over the full 20-week treatment period in patients with LGS.[a]



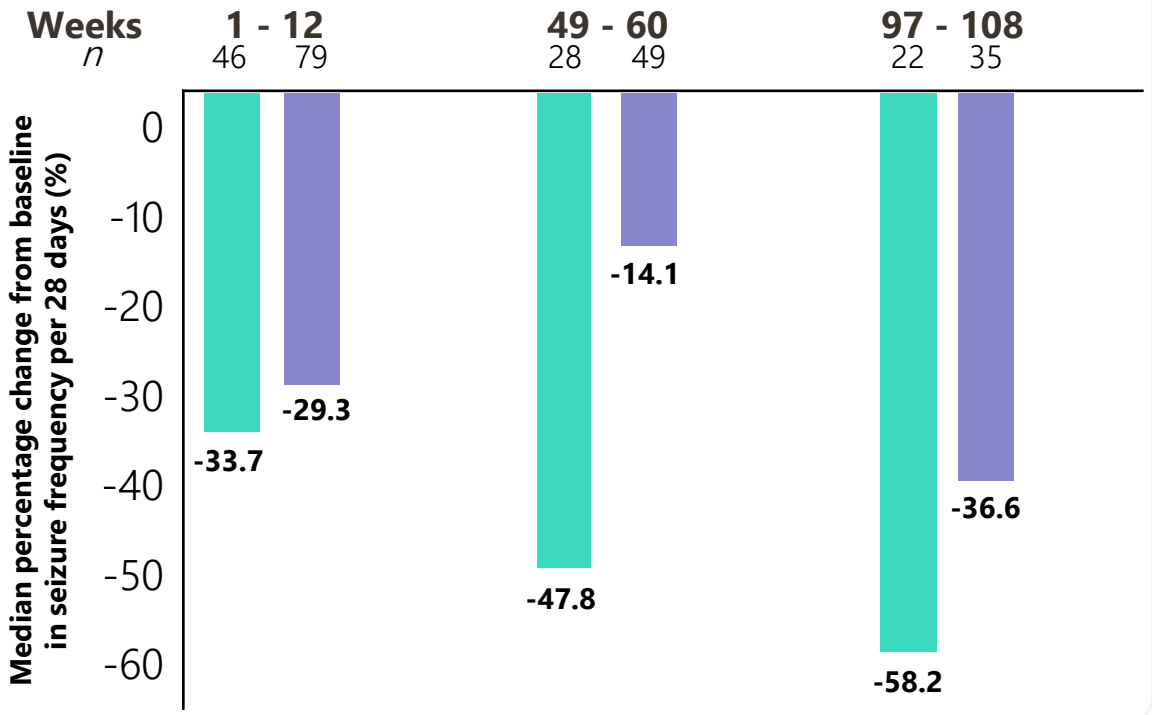
[a]Only data on seizure types observed in at least five patients in a treatment group are shown. Error bars represent first to third quartiles.
LGS, Lennox–Gastaut syndrome; Q1, first quartile; Q3, third quartile.

1. Efficacy of Soticlestat Treatment by Seizure Type in Patients with Dravet Syndrome or Lennox–Gastaut Syndrome in a Phase 2, Randomized, Placebo-controlled Study (ELEKTRA), Presented at AAN 2023: https://www.aan.com/MSA/Public/Events/AbstractDetails/53067

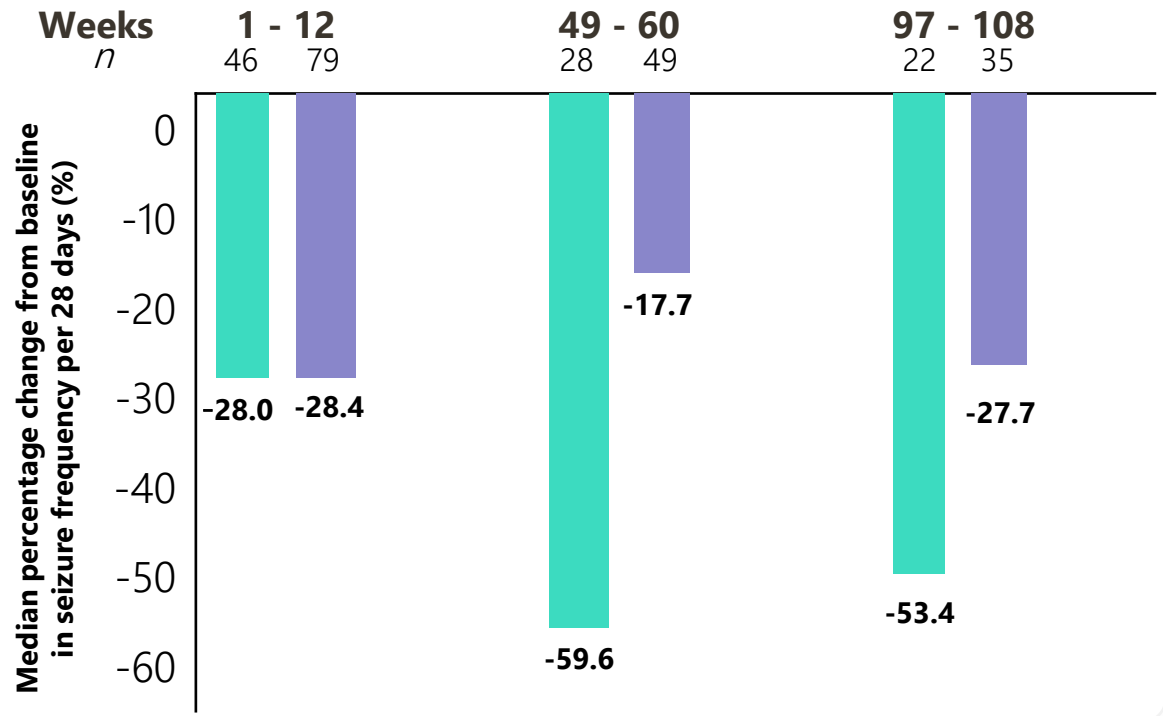
OLE (ENDYMION1): Sustained seizure reduction shown in DS & LGS patients up to 2 years[1]

Dravet syndrome Lennox Gastaut syndrome

Reduction in frequency of convulsive seizures for DS & drop seizures for LGS



Reduction in all seizure frequency



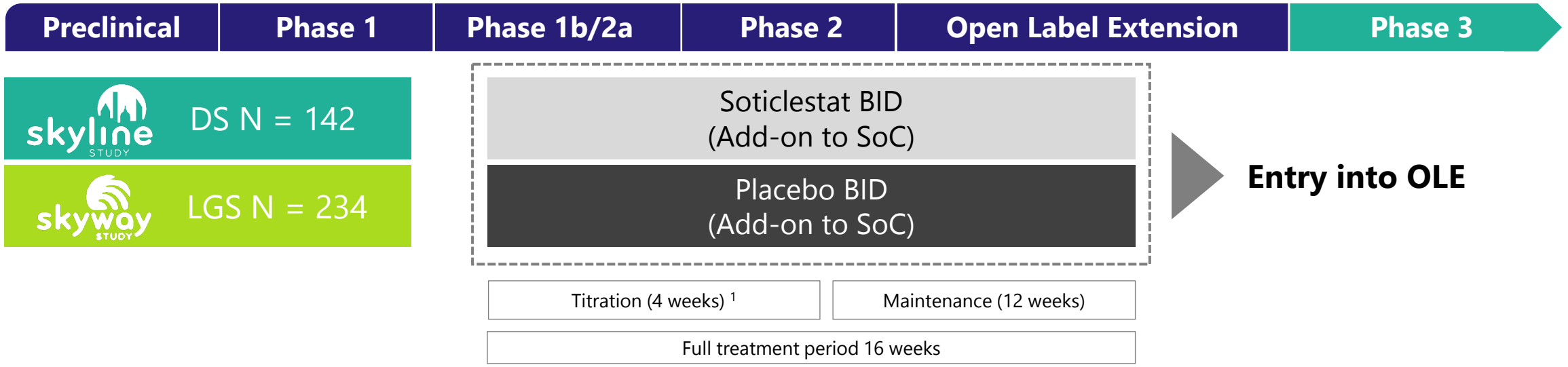
Soticlestat demonstrated up to 2 years of treatment and:

- Contributed to a sustained reduction in convulsive seizures in DS patients and drop seizures in LGS patients, which are similar endpoints being used in two pivotal Phase 3 trials ongoing in the same epilepsies
- Was associated with a reduced seizure frequency up to 2 years of treatment

1.: Long-Term Treatment Effects of Soticlestat in Patients with Dravet Syndrome or Lennox–Gastaut Syndrome: Interim Data from the ENDYMION 1 Trial as presented at AAN: https://www.aan.com/MSA/Public/Events/AbstractDetails/52787

Phase 3 pivotal trials

(Conducted by Takeda)



TRIAL DESIGN

- Trial design based on feedback from FDA, EMA & PMDA
- Ages ≥ 2 years
- Adjunctive to ASMs
- Active seizures at baseline[2]

[1]100 mg BID, 200 mg BID, 300 mg BID (mg/kg dosing)
[2]Clinical Trials.gov Accessed October 26, 2021.

OUTCOME MEASURES

Primary

- Frequency change in convulsive seizures (DS study) during full treatment period
  - DS: ≥4 convulsive seizures at baseline
- LGS study uses **Major Motor Drop seizure endpoint** (frequency change in major motor drop seizures) during full treatment period
  - LGS: ≥8 Major Motor Drop (MMD) seizures at baseline.
  - For LGS, countable drop seizures reliably recognized by the caregivers and consistently implemented by the investigators

Takeda anticipates global regulatory filing during its FY 2024 (April 1, 2024 – March 31, 2025)

The soticlestat opportunity

- Market research supports potential use as an early line option for patients not well-controlled on other antiseizure medications:
- Anticipated profile:[1]
  - ✓ Efficacy on top of standard of care therapies
  - ✓ Fewer side effects
  - ✓ No clinically relevant drug-to-drug interactions
  - ✓ No expected monitoring requirements
  - ✓ Promising safety profile

LARGE GLOBAL MARKET OPPORTUNITY[2]

~110-135K
Lennox-Gastaut syndrome
(7 major markets)

~30-45K
Dravet syndrome
(7 major markets)

If soticlestat is approved and commercialized, subsequent milestones and royalties may create a significant stream of non-dilutive capital to fund Ovid's pipeline

1) Hahn et al. A phase 2, randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of soticlestat as adjunctive therapy in pediatric patients with Dravet syndrome or Lennox–Gastaut syndrome (ELEKTRA). Epilepsia. 2022; 00: 1–13. https://doi.org/10.1111/epi.17367
2) Ovid Global Market Reseach 2022

OV888

A highly selective ROCK2 inhibitor for potential treatment of cerebral cavernous malformations (CCM) & other CNS disorders

ROCK2 inhibition: OV888 (lead program, formerly GV101)

UPDATE

Initiated multiple ascending dose study

- Studying pivotal gel capsule formulation
- No SAEs observed

Intend to initiate signal-finding trial in H2 2024

- Strong mechanistic rationale for ROCK2 signaling pathway in multiple CNS indications
- Blood-brain barrier penetrant in preclinical studies
- Well characterized safety profile in humans
- Most highly selective inhibitor for ROCK2 (not ROCK1) that is known[1,2]
- **Potential to be 1st disease modifying treatment for cerebral cavernous malformations (CCM)**

1) Based upon animal models
2) Ann Clin Transl Neurol. 2014 Jan; 1(1): 2–14. Published online 2013 Nov 19.

Cerebral cavernous malformations

Presentation & prevalence

- Mulberry-shaped abnormal blood vessels with thin, leaky walls located in the brain and or spinal cord, which increase over age
- CCM's among the most common intracranial vascular malformation in humans[1,2]

CCMs located in the brainstem pose unique challenges

- Brainstem CCMs are a key risk factor for brain bleeds, can cause significant morbidity due to repeated hemorrhaging[3]
- 82% of patients with brainstem lesions involve major fiber tracts, making surgery extremely difficult[3]
- Guidelines indicate that surgical resection of brainstem CCM could be considered only after a second symptomatic bleed given risks associated with the surgery[4]
    - Post operative mortality and morbidity are high among patients who undergo surgery to remove brainstem lesions[4]
    - 53% of the cases experience post operative neurologic deficits[2]

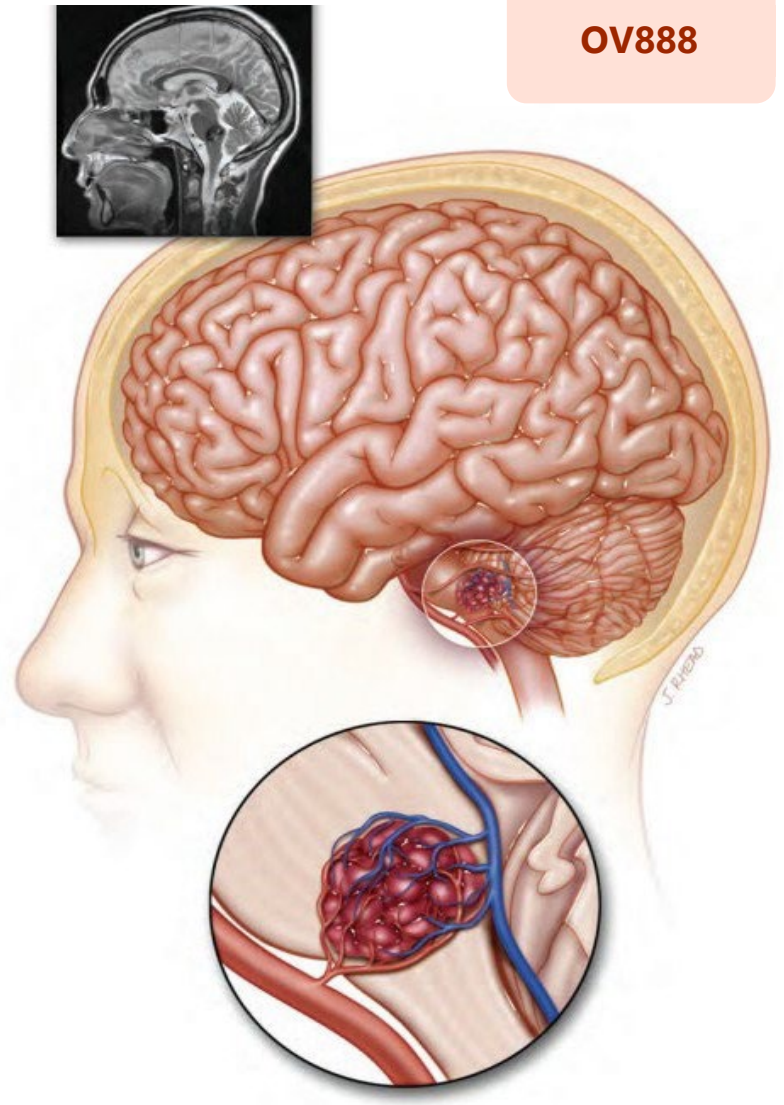
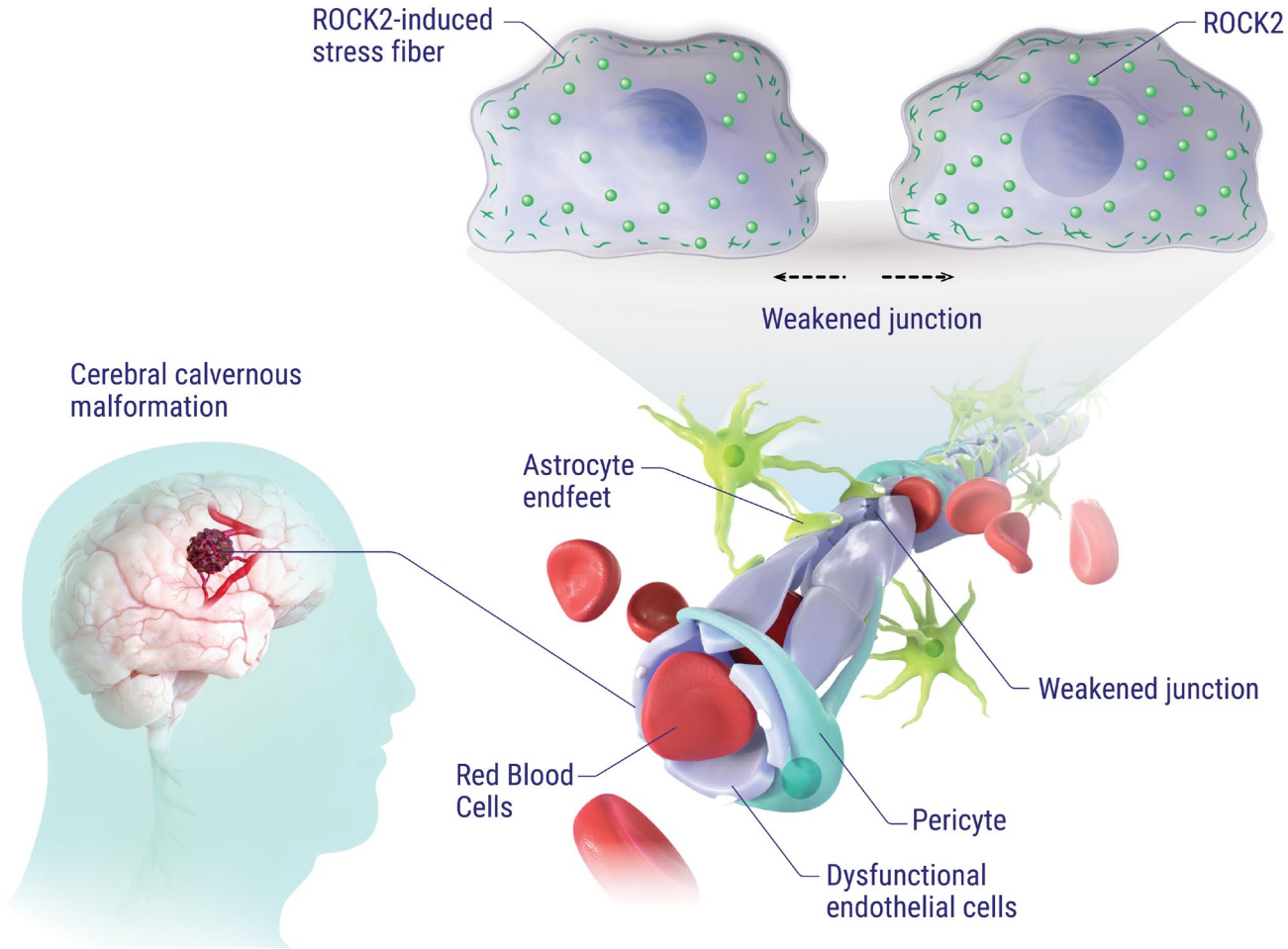


Image attribution: Brainstem angioma from Alliance to Cure Cavernous Malformation

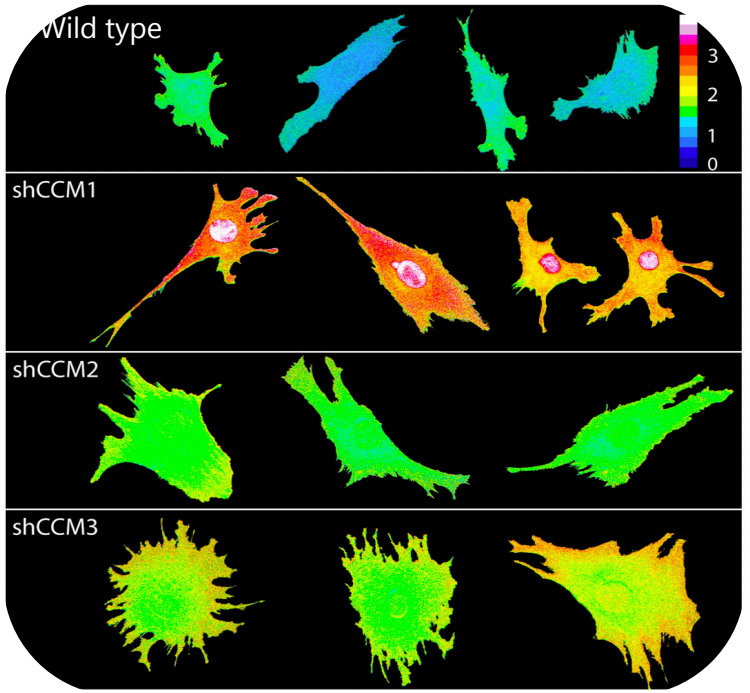
1. Zafar A, Quadri SA, Farooqui M, Ikram A, Robinson M, Hart BL, Mabray MC, Vigil C, Tang AT, Kahn ML, Yonas H, Lawton MT, Kim H, Morrison L. Familial Cerebral Cavernous Malformations. Stroke. 2019 May;50(5):1294-1301. doi: 10.1161/STROKEAHA.118.022314. PMID: 30909834; PMCID: PMC6924279 | 2. Caton MT, Shenoy VS. Cerebral Cavernous Malformations. [Updated 2022 Oct 3]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK538144/. | 3. Ma L, Zhang S, Li Z, Wu CX, Wang Z, Zhan L, Hao Q, Wang H, Ye X, Chen X, Liu YO, Wang S, Zhao YL. Morbidity After Symptomatic Hemorrhage of Cerebral Cavernous Malformation: A Nomogram Approach to Risk Assessment. Stroke. 2020 Oct;51(10):2997-3006. doi: 10.1161/STROKEAHA.120.029942. Epub 2020 Sep 21. PMID: 32951540. | 4. Akers A, Al-Shahi Salman R, A Awad I, Dahlem K, Flemming K, Hart B, Kim H, Jusue-Torres I, Kondziolka D, Lee C, Morrison L, Rigamonti D, Rebeiz T, Tournier-Lasserve E, Waggoner D, Whitehead K. Synopsis of Guidelines for the Clinical Management of Cerebral Cavernous Malformations: Consensus Recommendations Based on Systematic Literature Review by the Angioma Alliance Scientific Advisory Board Clinical Experts Panel. Neurosurgery. 2017 May 1;80(5):665-680. doi: 10.1093/neuros/nyx091. PMID: 28387823; PMCID: PMC5808153.

Illustrative cerebral cavernous malformation (CCM) brain



Endothelial cytoskeleton abnormalities & weakened cell junctions can lead to lesions and bleeds

EXAMPLE AT CELLULAR LEVEL

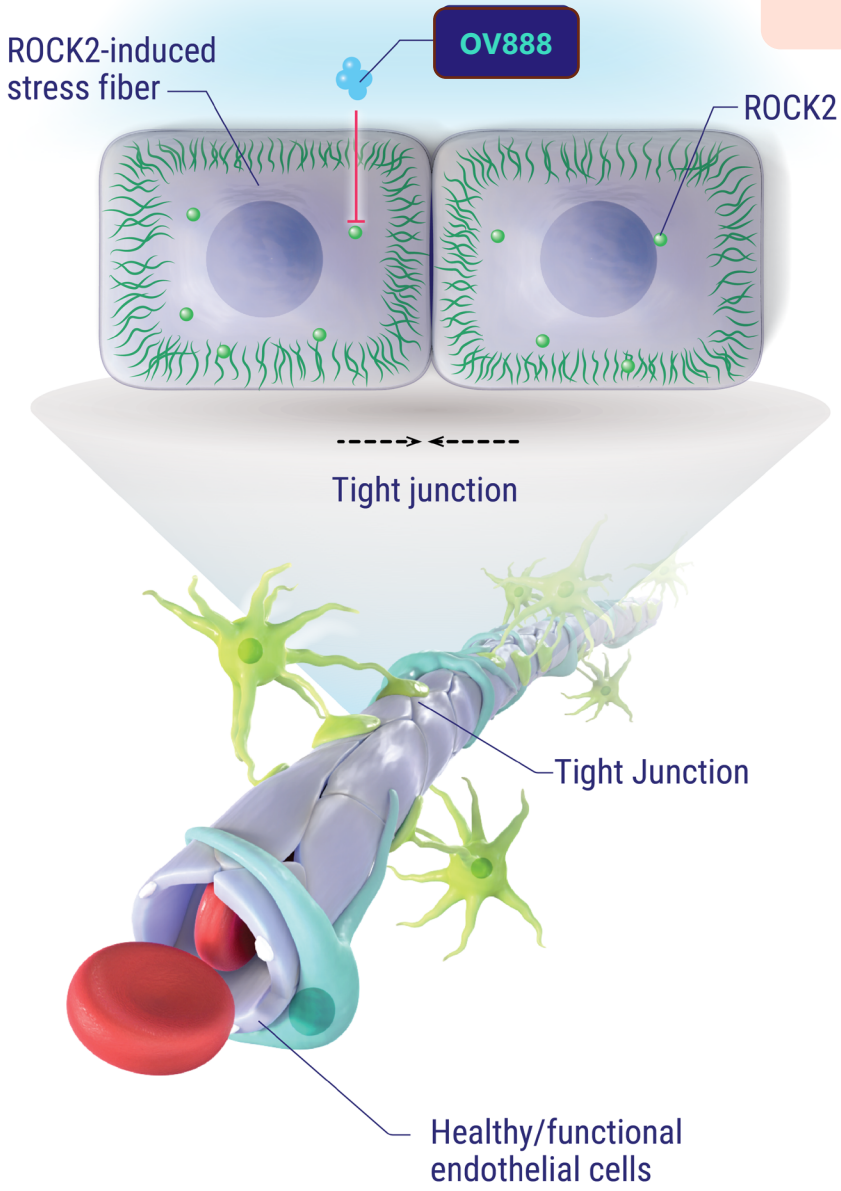


Relative to wild type (healthy) cells CCM exhibits cellular mis-formation due to stress fibers[1]

1. A. L. Borilkova, et. al (2010) Journal of Biological Chemistry, Vol 285. 11760 and O. Pertz, et al (2006) Nature, Vol 440:1069

Believed mechanism of action for OV888

- Inhibits ROCK2
- Returns extracellular matrix and tube formation to more normalized state
- **Thereby, anticipated to help stabilize and shrink cavernoma lesions**



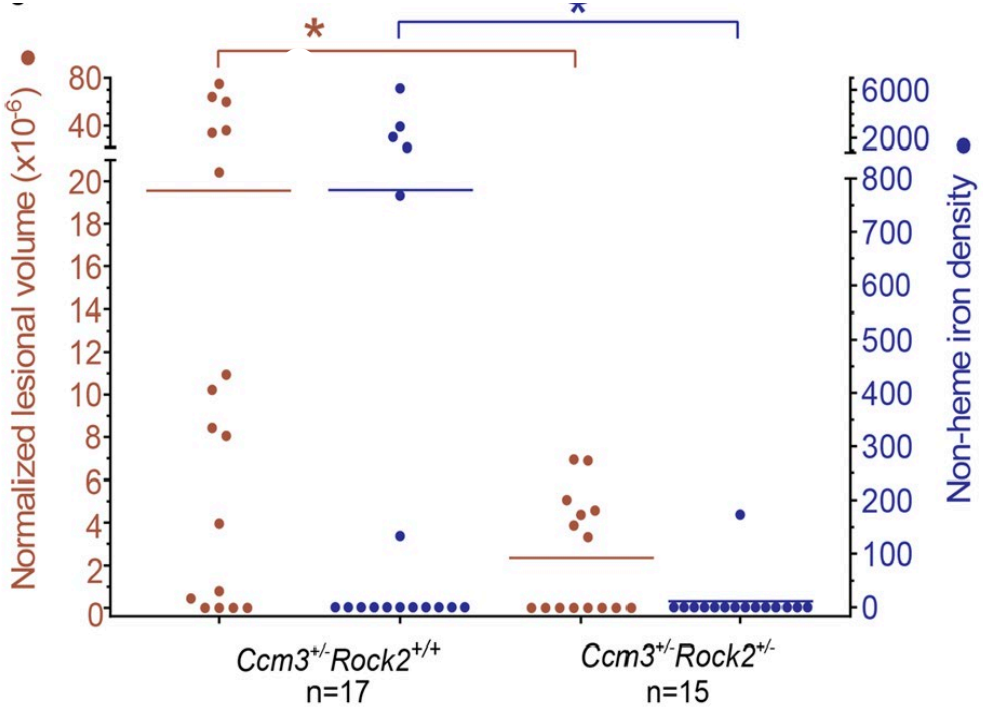
Validation of ROCK2 vs. ROCK1 as targets for CCM

ROCK2$^{+/-}$, not *ROCK1*$^{+/-}$ mice have lower cavernous angiomatosis[1]

Transgenic mouse model of CCM3

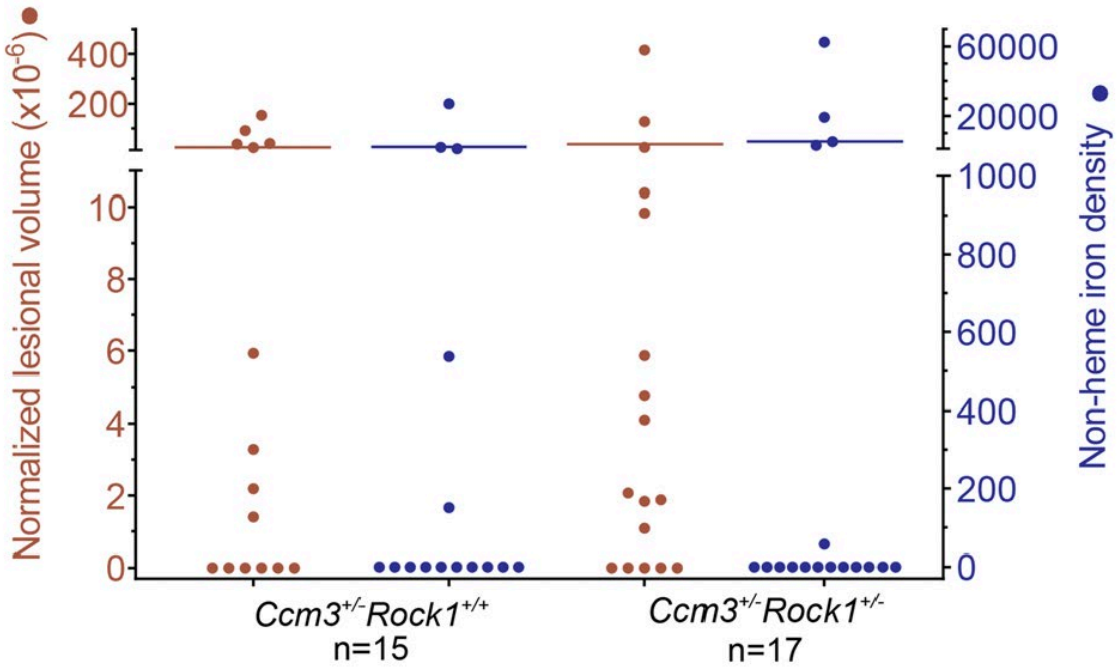
ROCK2:

Rescue effect & reduced a marker of hemorrhage



ROCK1:

No rescue effect



1. McKerracher L.; et. al. Translational Stroke Research (2020) 11:365-376

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

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

Chart based on biochemical assays

Molecules with pan-ROCK inhibition have shown off-target effects

1 Ann Clin Transl Neurol. 2014 Jan; 1(1): 2–14. Published online 2013 Nov 19. doi: 10.1002/acn3.19

2 https://patents.google.com/patent/US10106525B2/en

OV888 clinical development update

PRIOR PHASE 1: NANO-SUSPENSION

Single & multiple ascending dose study in healthy adult volunteers in 2022

- Double-blinded, placebo controlled
- 50 male/female healthy adult volunteers
- 7-day consecutive dosing:
  - SAD: 400 mg, 800 mg, and 1200 mg
  - MAD: 200 mg and 400 mg
- Endpoints: Safety & tolerability; PK
- Findings:
  - 0 SAEs
  - AE of interest (headache (21%), diarrhea (11%), CPK elevations (6%) nausea/vomiting (2%)
- Similar AUC to U.S. study (AUC 11,600 in 1,200 mg group)

PROGRESS UPDATE: OV888 CLINICAL FORMULATION

Timing:
- Initiated multiple ascending dose trial in Q3

Objective:
- Confirm safety and establish maximum dose tolerated

Approach:
- Randomized, placebo-controlled, double-blind, single-center MAD
- 8 per dose group; 3:1 randomization
- 7-day dosing, 72-hour trailing PK data collection

Status:
- No serious adverse events

Next steps:
- Complete multiple ascending dose program
- Requesting FDA pre-IND meeting

OV329

A next-generation GABA-aminotransferase inhibitor for the potential treatment of pharma-co resistant seizures

OV329: Large opportunities

UPDATE

Phase 1 SAD (3 cohorts complete)
- No safety signals
- Dose escalating

Expanding formulations
- Oral
- Intravenous

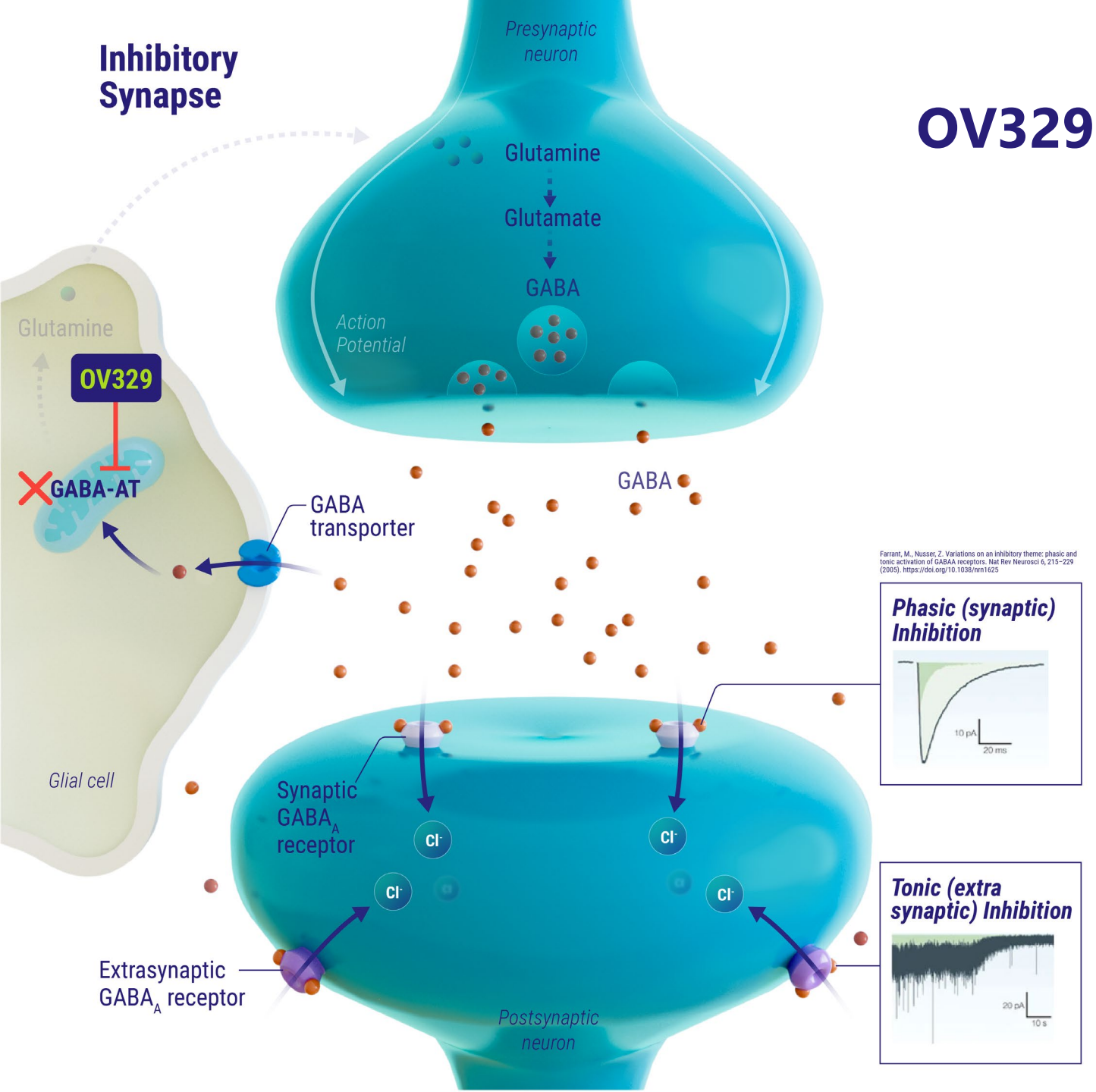
Expanding development program

Multiple potential indications
- Chronic
- Acute

- Unique molecule for a validated target, GABA aminotransferase (GABA-AT)
- Promotes inhibitory neurotransmitter (GABA) to reduce seizures
- Established therapeutic window[1]
  - Prior GABA-AT inhibitor, vigabatrin, had no window
- Phase 1 study - exploring safety & surrogate biomarker for efficacy
- New findings support low, repeat dosing:[1]
  - Prolonged effects in seizure reduction
  - Ability to maintain optimal levels of GABA
  - Sustained shifts of tonic and phasic current
  - Established a PD marker for human studies
- OV329 may have utility in acute seizures in addition to chronic

1) In animal models

OV329 mechanism of action



- GABA is the major inhibitory neurotransmitter in brain
- OV329 substantially reduces GABA-AT activity, a key enzyme responsible for degrading GABA, thus elevating GABA levels
- OV329 increases phasic and tonic inhibitory neurotransmission at GABAergic synapses
- Curbs excessive neuronal excitation and reduces seizures

OV329 development program

Potential for chronic and acute treatments (via oral & IV formulations)

ORAL – CHRONIC DOSING

- Three SAD cohorts completed in healthy volunteers
  - No safety signals found
  - Moving to MAD
  - Adding site for the Phase 1 SAD/MAD
- Pursuing simultaneous demonstration of anti-convulsant utility via simultaneous transcranial magnetic stimulation (TMS) study
- Conducting animal models to further differentiate PK/PD and safety from vigabatrin

IV – ACUTE DOSING

- Formulating OV329 in IV
- Initiated toxicology for acute dosing
- Intend to initiate a status epilepticus signal finding trial in 2025

OV329 anticipated profile

OV329 PROFILE

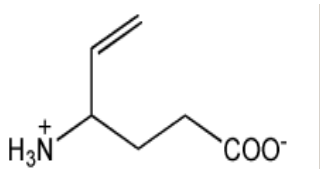
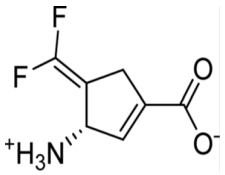
Significant potency expected to deliver enhanced

- ✓ Efficacy
- ✓ Safety
- ✓ Lower dosing

Optimal levels of GABA for sustained seizure suppression

- ✓ Delivers anti-convulsant effects at very low doses
- ✓ Repeated (chronic) low doses deliver sustained seizure reduction and profound changes in tonic (extra-synaptic) inhibition
- ✓ EEG measurements confirm anti-convulsant properties at very low doses
- ✓ Tissue accumulation of OV329 is expected to be less than vigabatrin

OV329 profile differentiates from vigabatrin

	Vigabatrin	OV329
Molecule		
Potency	IC_{50}: ~60 – 100 μM	IC_{50}:~0.1 - 0.3 μM
Exposure characteristics	$T_{1/2}$ >5.0 Hours Both R (inactive) & S (active) enantiomers	Reduced exposure ($T_{1/2}$ ~1.0 Hour) coupled with prolonged PD duration
Mechanism of enzyme inhibition	Covalent modification of GABA-AT (early generation chemistry, primarily Michael addition pathway) [1]	Electrostatic (more sophisticated chemistry, primarily enamine pathway) [2]
Purity	Racemase (mixture of active (S) and inactive (R) enantiomers)	Only active, S form
Therapeutic window in Sprague Dawley rats (a proxy model used to assess ocular safety)	✗ None – toxicity seen at therapeutic dose of 300 mg/kg	✓

1. J Med Chem. 2012 Jan 26; 55(2): 567–575; 2. J Am Chem Soc. 2018 Feb 14; 140(6): 2151–2164

Development plans

	DEVELOPMENT	POTENTIAL INDICATIONS
OV329 Oral formulation	• Initiating multiple ascending dose cohorts • Expect higher dose escalation in humans • Concurrent TMS study to demonstrate PD • Measuring target engagement surrogate biomarker via MRS (vs VGB) • Concurrently assessing back of eye accumulation vs VGB in animals • **Timing**: Full readout H2 2024	• Tuberous sclerosis seizures • Infantile spasms • Conditions with focal seizures
OV329 IV formulation	• Formulating OV329 for IV • Conducting supportive animal toxicology & disease models	• Status epilepticus • Refractory status epilepticus

KCC2 library & OV350

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

KCC2 direct activation: OV350 (lead program)

UPDATE

1st IND for OV350 in resistant epilepsy anticipated for H2 2024

- Planning for intravenous formulation initially
- Intend to pursue an oral formulation

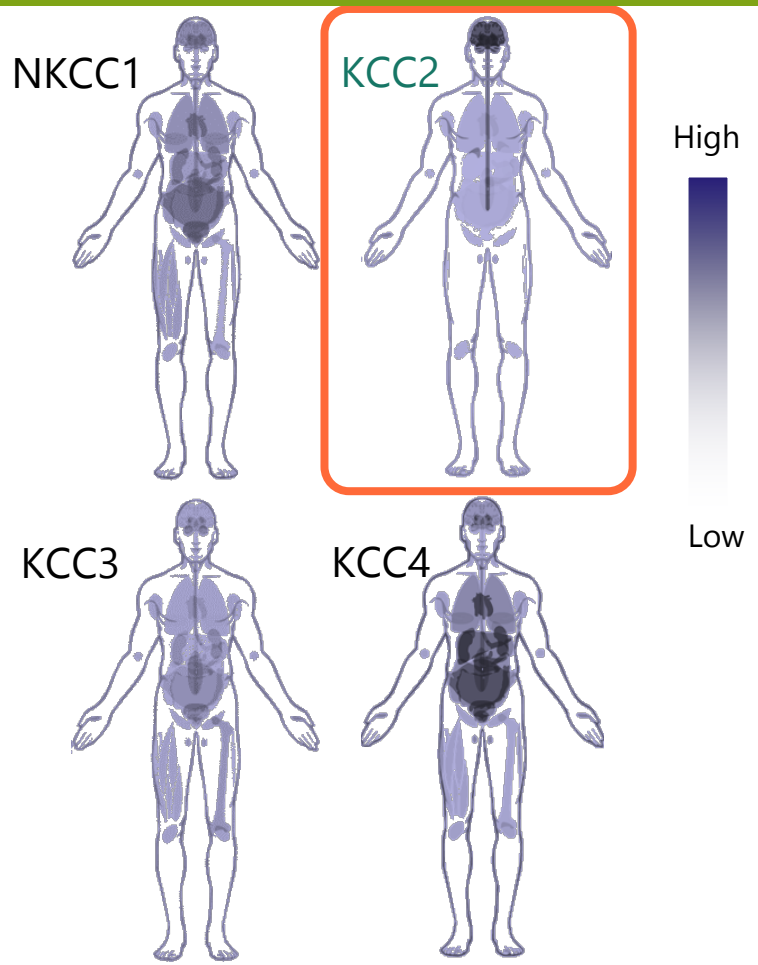
New animal findings

Broad therapeutic potential in CNS conditions

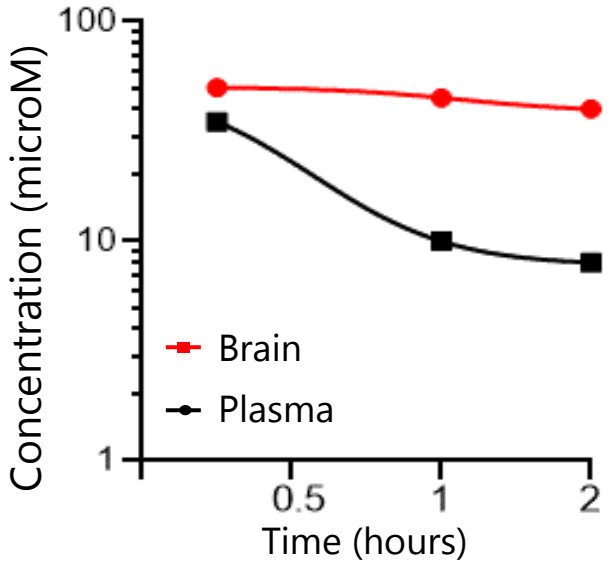
- Library of ~100 compounds that are direct activators of potassium chloride co-transporter 2 (KCC2)
  - Unique compounds offer discrete properties
  - Amenable to intravenous, oral and injectable formulations
- Represent a potential franchise of neurotherapeutics
- Activators directly modulate intrinsic hyperexcitability of neurons via chloride extrusion
- Animal models of disease have confirmed
  - Anti-convulsant properties as monotherapy and as a potentiator
  - Anti-psychotic and anti-schizophrenic properties
  - No sedative effects at expected therapeutic windows

OV350 shows rapid, stable accumulation in the brain with a translatable pharmacodynamic biomarker[1]

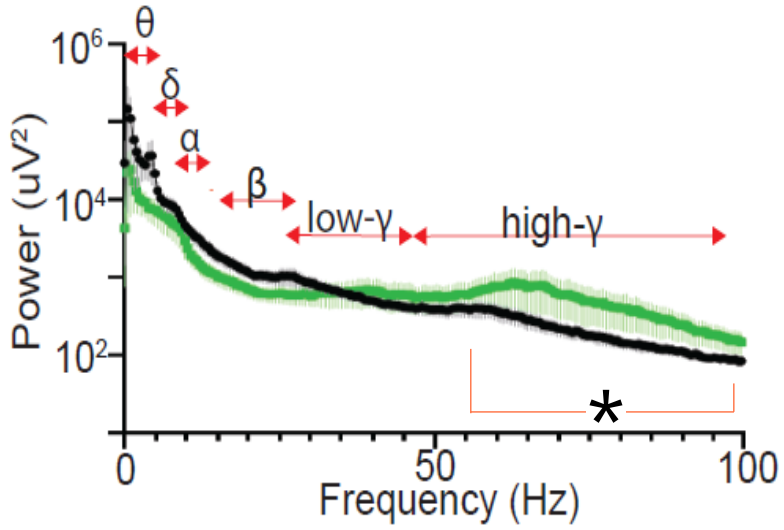
A. KCC2 is expressed exclusively in neurons



B. OV350 rapidly accumulates in rodent brain via IV/IP dosing



C. OV350 induces a shift in EEG high gamma power spectrum (biomarker)



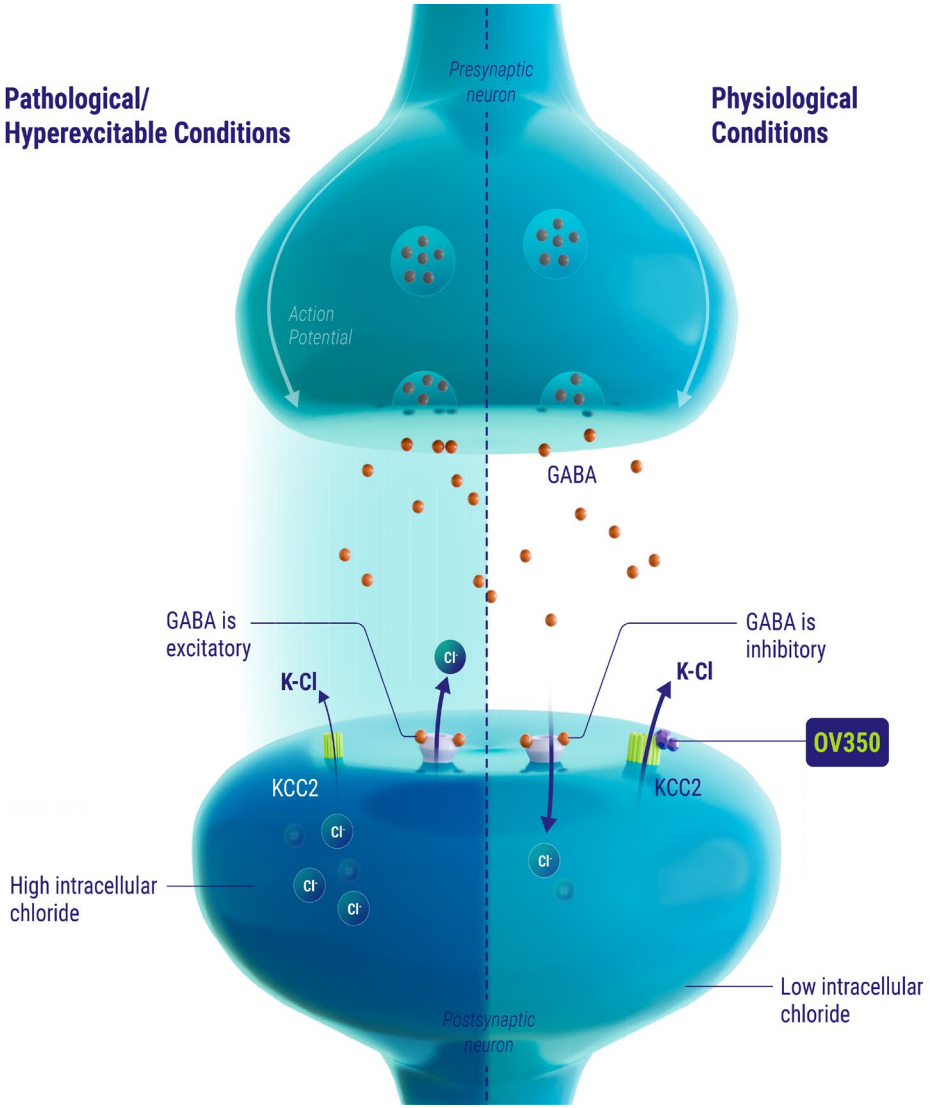
- OV350 in-vivo pharmacokinetics shows high micromolar accumulation in the brain within minutes
- Highly translatable EEG pharmacodynamic biomarker confirmed in healthy animals[1]

1. Ovid data on file

OV350 mechanism of action

Impaired KCC2 activity

- Causes high intra-neuronal chloride concentrations leading to abnormal depolarizing of the GABA receptor
- Causes neuronal hyperexcitability leading to epilepsy seizures and other pathologies



In normal KCC2 activity

- NKCC1 activity is low while KCC2 activity is high leading to low intra-neuronal Cl− concentration
- Enables a GABA-driven influx of Cl−, causing an inhibitory effect (hyperpolarizing) to the GABAA current

OV350 directly activates KCC2 transporter, improving chloride extrusion and improving neuronal inhibition in preclinical models

In-vivo preclinical POC data for OV350 in epilepsy

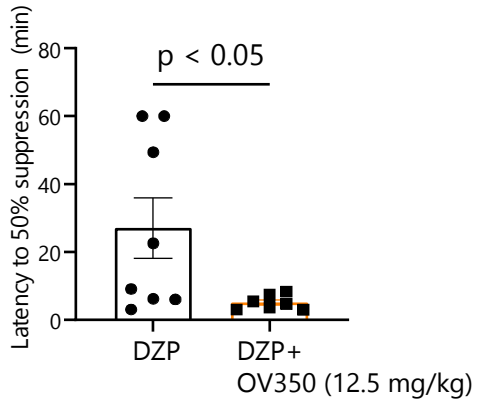
OV350 terminates ongoing and benzodiazepine refractory status epilepticus

- OV350 demonstrated anti-seizure activities in kainate challenge model
- Mice implanted with electrodes to measure kainate induced seizures and demonstrated that OV350 at 50mg/kg and 12.5mg/kg
  - Restored diazepam activities in stopping seizures
- Supports development in Status Epilepticus using IV formulation of OV350/Benzodiazepine combination

INDUCTION OF STATUS EPILEPTICUS (SE)

EEG traces show SE cessation after OV350 intervention with DZ

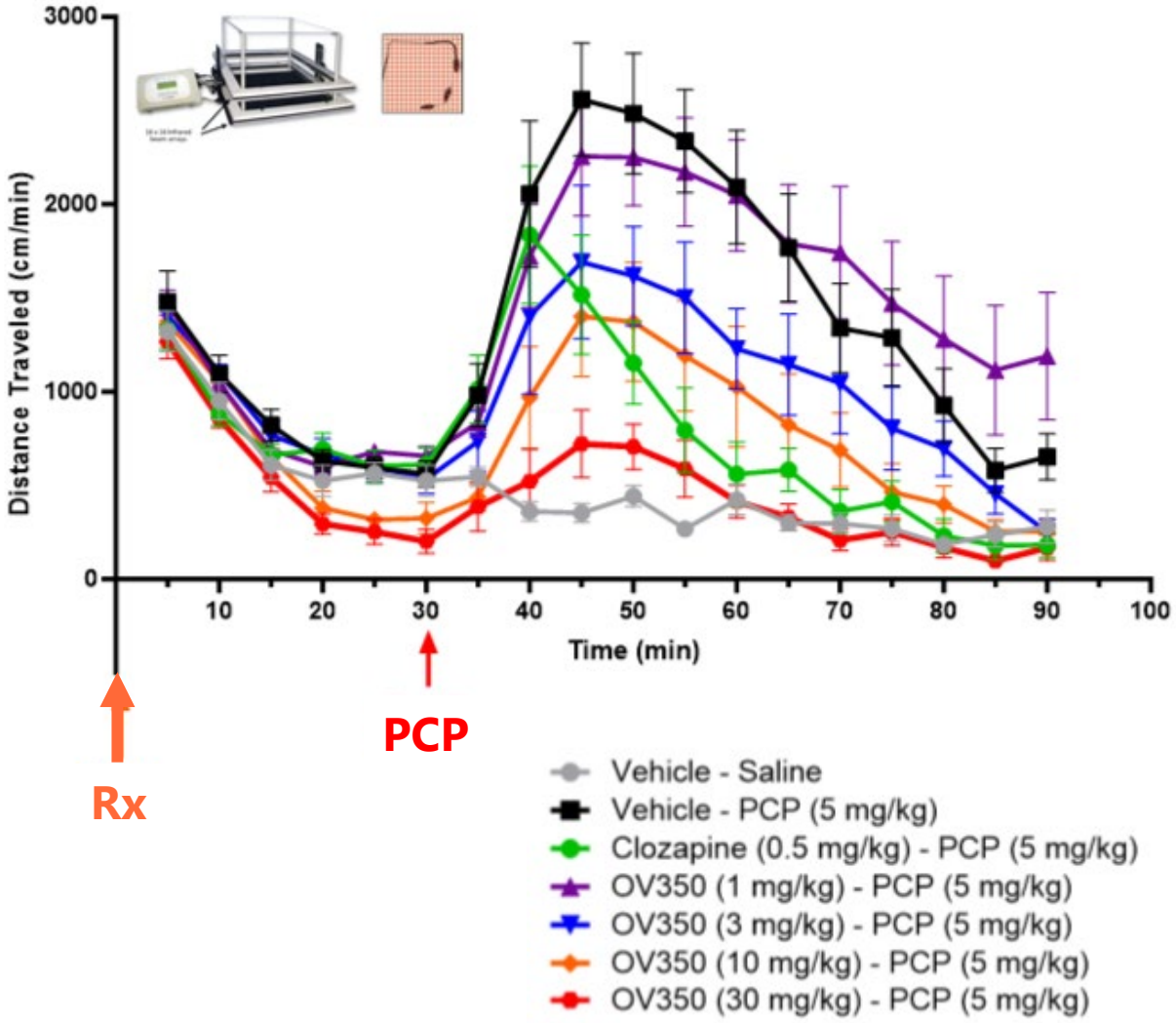
EFFICACY CONFIRMED AT A LOWER DOSE



OV350 restores the activity of Diazepam in drug-refractory seizures

Jarvis et al., 2023, Cell Reports Medicine 4, 100957; [2]PNAS, 2015;112:3523; [3]Unpublished data

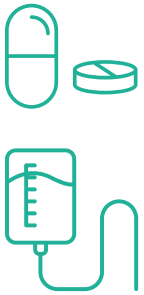
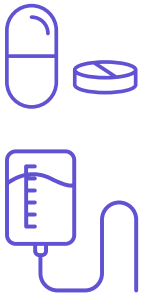
OV350 anti-psychotic effects demonstrated in a schizophrenia model



- Phencyclidine-induced psychosis is characterized by:
  - Confusion, excitation, aggression, paranoia, hallucinations, and can be experimentally measured by hyperlocomotion
- Phencyclidine challenge is a widely used as model for schizophrenia
- OV350 inhibited PCP induced hyperlocomotion with clear dose dependent responses
- OV350 appears to have anxiolytic effects without causing sedation

OVID data on file

Development plans

	DEVELOPMENT	POTENTIAL INDICATIONS
 **OV350 anti-convulsant applications**	• Conducting IND-enabling animal toxicology for current IV formulation • Formulating additional oral and injectable formulations • **Expected IND filing for IV: H2 2024**	• Status epilepticus (IV) • Oral (multiple acute and chronic resistant seizure conditions)
 **OV350 anti-psychotic applications**	• Conducting further animal disease models • Oral formulation and toxicology ongoing • Characterizing additional KCC2 activator compounds	• Psychosis • Schizophrenia • Depression

Robust near-term news flow of clinical & regulatory milestones

Cash runway supports programs to and through de-risking milestones

PROGRAM	MILESTONE	ANTICIPATED TIMING
Soticlestat	Phase 3 data for Lennox-Gastaut syndrome Phase 3 data for Dravet syndrome	Prior to regulatory filings in Takeda FY 2024 Estimated trial completion dates on www.clinicaltrials.gov
	Regulatory submissions for Lennox-Gastaut syndrome and Dravet syndrome	Takeda's FY 2024 (April 2024 – March 2025)
OV888	Complete Phase 1 MAD study	H1 2024
	Initiate signal-finding trial in CCM	H2 2024
OV329	Phase 1: SAD/MAD with MRS biomarker and TMS (chronic)	H2 2024
	IND for IV formulation (acute)	H2 2024
KCC2 & OV350	IND submission (IV formulation)	H2 2024

FOCUSED PIPELINE
to treat epilepsy &
conditions with seizure symptoms

HARNESSING A REVOLUTION
in targeted small molecules for
the central nervous system

NOVEL BIOLOGICAL TARGETS
implicated in the balance of neuronal
excitation/inhibition or underlying
structural conditions

UNIQUE MECHANISMS OF ACTION
To deliver potential anti-seizure medicines
with preferable efficacy,
safety & tolerability

POTENTIAL TO PARTNER
non-epilepsy indications and ex-U.S. rights

CAPITAL ANTICIPATED TO FUND
programs through major de-risking events