Ovid Therapeutics

Corporate Overview

(NASDAQ: OVID)

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SEPTEMBER 2022

Disclaimers and forward-looking statements

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 preclinical data 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 and OV350; the likelihood that data for OV329 will support future development and therapeutic potential; the potential development of 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 timing for filing of the Company's IND applications; the timing for the completion of Takeda's two pivotal Phase 3 trials evaluating soticlestat for Lennox-Gastaut and Dravet syndromes; 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, OV350, 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," "plan", "believes", intends," "anticipates," "strives," "pursue," "design," "advance," "target," "seek" and "expects."

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 presented by the ongoing COVID-19 pandemic. 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 on Form 10-Q filed with the Securities and Exchange Commission (SEC) on August 9, 2022, 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.

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Transforming the lives of individuals with epilepsies & rare neurological diseases

+ Pipeline dedicated to addressing **significant unmet need & large addressable market** in epilepsies & neurological diseases

+ **Significant financial interest in soticlestat** currently in Phase 3 development by Takeda

Ovid™ Therapeutics

+ **Veteran team** with track record of value creation

+ **Cash runway into 2025** & disciplined approach to business development

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Team of disciplined operators, value creators

Management Team



Jeremy Levin
D. Phil, MB BChir
Chairman, CEO



Julia Tsai, Ph.D.
Head Clinical Development & Medical



Claude Nicaise, M.D.
Head, Research & Development



Jason Tardio, MBA
Chief Operating Officer



Jeffrey Rona
Chief Business & Financial Officer



Tom Perone, MBA, J.D.
General Counsel, Corporate Secretary, Chief Compliance Officer



Meg Alexander
Chief Corporate Affairs Officer



Luke Rosen
Head, Accelerated Development Community Engagement

Transformative transactions

- Invested ~$75M in soticlestat for $196M upfront payment and potential milestones & royalties of $650M+

Track record of expedited development

- Completed soticlestat Phase 2 six months ahead of schedule and under budget

Experience from 25+ launches, including 4 CNS blockbusters

Deep knowledge from development & launch of multiple epilepsy medicines

Contributed to development & launch:

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Advancing epilepsy franchise & genetic seizure programs

Small molecule

Genetic target

EPILEPSY PROGRAMS	INDICATION/TARGET	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	ANTICIPATED MILESTONES
OUT-LICENSED TO Takeda **SOTICLESTAT** CH24H inhibitor	Dravet syndrome					• Regulatory milestones • Sales milestones • Royalties
	Lennox-Gastaut syndrome					
OV329 GABA aminotransferase inhibitor	Tuberous Sclerosis Complex, Infantile Spasms and Focal Seizures					Anticipated IND in 2022
IN-LICENSED FROM AstraZeneca **OV350** KCC2 transporter activator	Resistant epilepsies and other neuro-pathologies					Anticipated IND in 2024

TARGETED CNS PROGRAMS	INDICATION / TARGET	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	MILESTONE
OV882 *Collaborator: UCONN*	Angelman syndrome					
OV815 *Collaborator: Columbia Univ.*	KAND – KIF1A associated-neurological disorders					
OV825 *Collaborator: Columbia Univ.*	HNRNPH2					
UNDISCLOSED GENE TARGETS WITH COLUMBIA UNIVERSITY						

STRATEGIC BUSINESS DEVELOPMENT ACTIVITIES FOCUSED ON COMPLEMENTING OUR GENETIC TARGETS & AUGMENTING CLINICAL STAGE ASSETS

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Epilepsy is a significant & growing market

WORLDWIDE…

~65M[1]
Patients

30-40%[3]
of individuals with epilepsy have seizures not controlled with antiepileptic drugs (AED)

>$8B[2]
Market

~6% per year
Branded AED market growth through 2025



3
million
adults living with epilepsy in the US[4]

470,000
US children
≤17 years have epilepsy[4]

Source:
1. WHO 2019
2. Global Data Report, Epilepsy: Global Drug Forecast and Market Analysis to 2030 – Forecast Update
3. Huron Primary Research (11/2019-12/2019)
4. CDC Epilepsy data: https://www.cdc.gov/epilepsy/data/index.html

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Medicines with novel mechanisms for epilepsies are needed

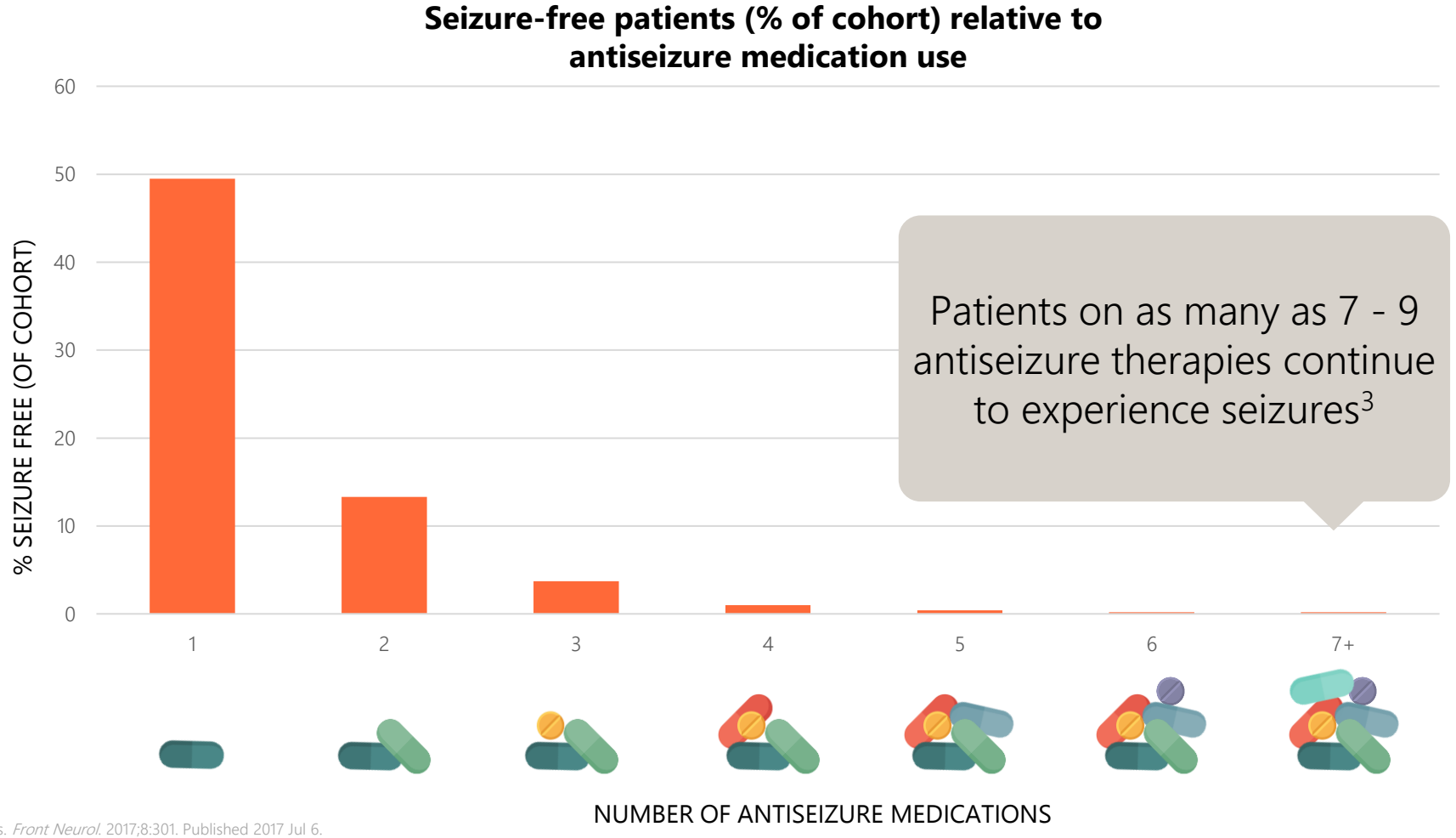
Many patients continue to experience seizures despite polypharmacy

~30%

of epilepsy patients
remain treatment-resistant
– continuing to experience seizures[1]

~47%

of epilepsy patients report
polypharmacy
– taking on average 5 medications[2]



1. Tang F, Hartz AMS, Bauer B. Drug-resistant epilepsy: multiple hypotheses, few answers. *Front Neurol.* 2017;8:301. Published 2017 Jul 6.
2. Terman SW, Aubert CE, Hill CE, et al. Polypharmacy in patients with epilepsy: a nationally representative cross-sectional study. *Epilepsy Behav.* 2020;111:107261.
3. Brodie MJ, Barry SJ, Bamagous GA, Norrie JD, Kwan P. Patterns of treatment response in newly diagnosed epilepsy. *Neurology.* 2012;78(20):1548-1554.

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Franchise of potentially novel epilepsy medicines

Programs with complementary potential best-in-class or first-in-class mechanisms of action

	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3

IN-LICENSED

OV329

Northwestern University

Potential best-in-class, oral GABA aminotransferase inhibitor with an enhanced benefit/risk profile and administration in preclinical development for focal seizures, tuberous sclerosis and infantile spasms

OV350 & KCC2 PLATFORM

AstraZeneca

Potential first-in-class KCC2 direct activator – and a library of novel, direct KCC2 activators for resistant epilepsies and other CNS indications in-licensed from AstraZeneca

OUT-LICENSED

SOTICLESTAT

Takeda

A novel 24-cholesterol hydroxylase inhibitor for Dravet & Lennox Gastaut syndromes out-licensed to Takeda in transaction that can generate up to $856M in total upfront & milestones payments (including $196M previously paid)[1]

[1] In 1H 2021

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OUT-LICENSED TO TAKEDA

OVERVIEW: soticlestat

Potential first-in-class cholesterol 24-hydroxylase inhibitor for treatment resistant epilepsies[1]

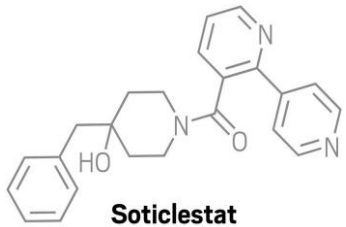
Actively being studied in two pivotal, Phase 3 trials

(conducted by Takeda):

- Dravet syndrome (DS)
- Lennox-Gastaut syndrome (LGS)

Designed to reduce seizure susceptibility & improve seizure control[2]

Well characterized mechanism of action



Soticlestat

- Reduces glutamatergic signaling & reduced inflammation[1,3]
- Dose dependent response[1,3]

Data to-date suggests potential use in early treatment lines[2]

- Based upon promise of seizure control efficacy and tolerability profile observed in clinical trials
- No monitoring anticipated for soticlestat as is required for other new anti-seizure medicines[4]

Encouraging safety and tolerability profile in Phase 2 trials[2]

- Main adverse events for soticlestat over placebo are lethargy/somnolence and constipation
- No anticipated monitoring needs

New drug applications planned by Takeda in its fiscal year 2024

[1] Nishi T, et al. AAN 2018. [2] 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 3. [3] Salamone A, et al. ECE 2018 [4] FINTEPLA prescribing information label, pages 5-8.

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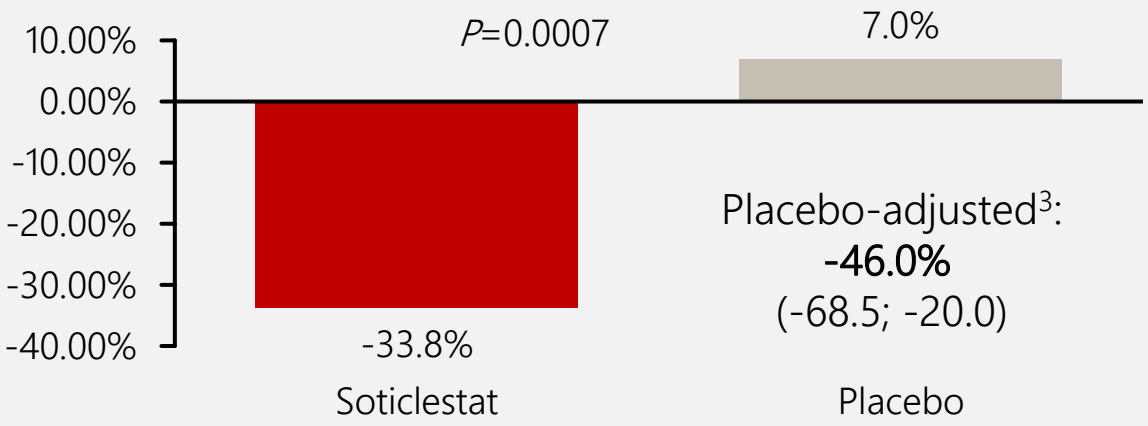
Soticlestat demonstrated statistically significant seizure reduction in Dravet syndrome; numeric reduction in Lennox-Gastaut syndrome[1]

soticlestat

DRAVET SYNDROME (CONVULSIVE SEIZURES)

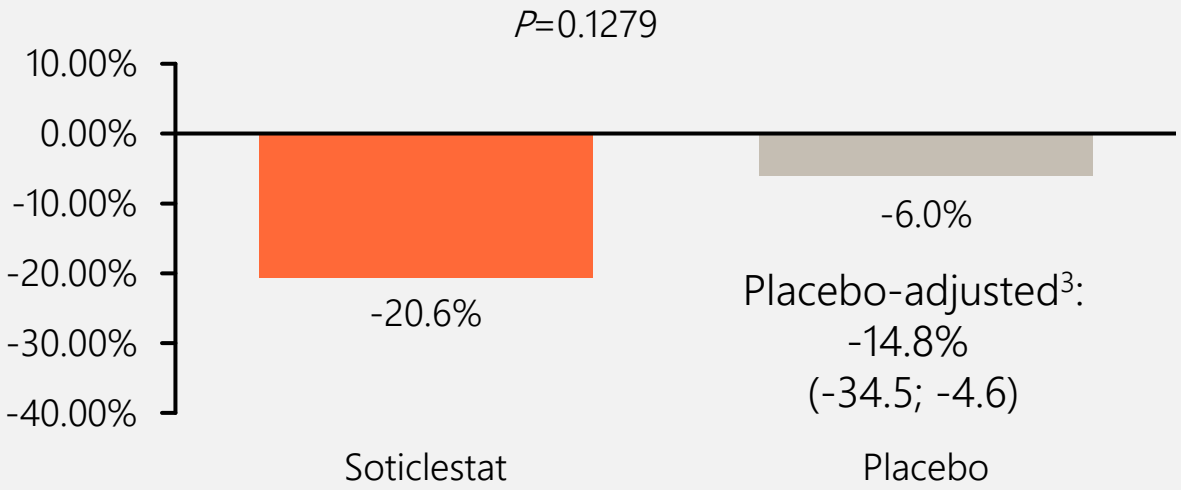
Median Change from Baseline in Seizure Frequency[2] During 20-week Treatment Period (mITT)



- Statistically significant placebo-adjusted median seizure reduction of 46%
- DS cohort was not powered for efficacy

LENNOX-GASTAUT SYNDROME (DROP SEIZURES)

Median Change From Baseline in Seizure Frequency[2] During 20-week Treatment Period (mITT)



- Placebo-adjusted median seizure reduction of 14.8% did not reach statistical significance; this was impacted by the LGS cohort using a broad definition of drop seizure frequency at baseline of 4 to >5,000 drop seizures/28 days
- A subsequent sensitivity analysis supportive of more stringent, countable drop seizure definition

[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] Asymptotic 95% confidence interval and Hodges-Lehmann estimation of the median of differences in % change between the two arms from un-adjusted rank statistics. The modified intent-to-treat (mITT) = All randomized subjects who received at ≥ 1 dose of study drug and were assessed for ≥1 day during treatment

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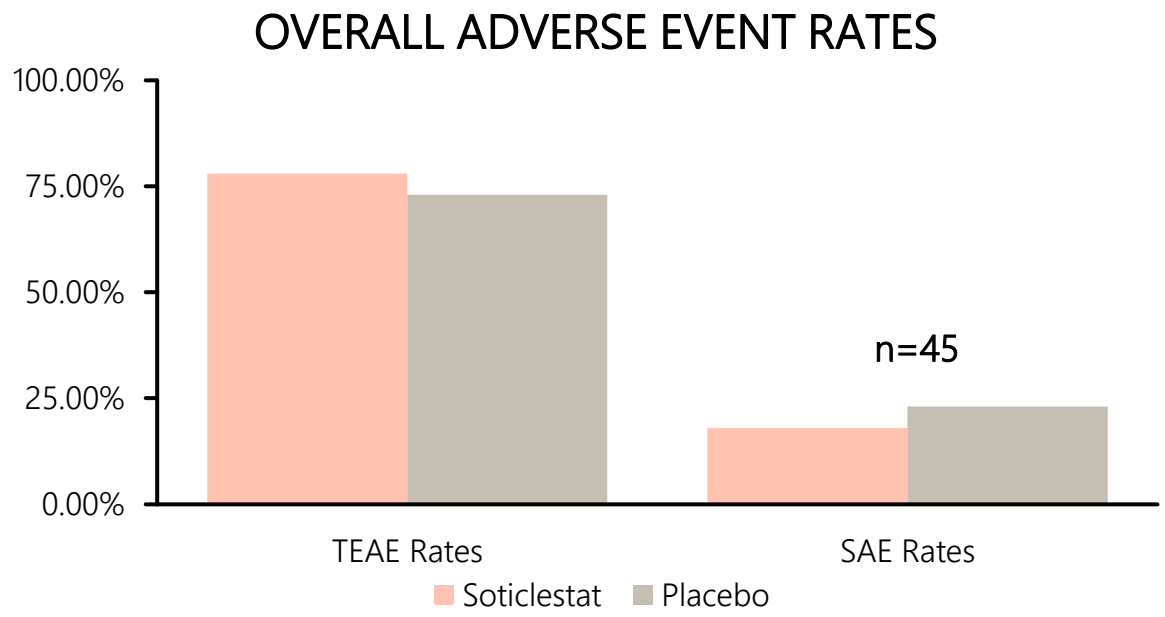
Encouraging safety & tolerability profile ELEKTRA TEAEs

TEAEs >5% in soticlestat & >3% difference from placebo	Soticlestat (n=71)	Placebo (n=70)
Pyrexia	11 (15.5%)	8 (11.4%)
Somnolence	6 (8.5%)	3 (4.3%)
Lethargy	5 (7%)	0 (0%)
Constipation	4 (5.6%)	0 (0%)



- Safety profile consistent with previous findings; no new safety findings
- TEAEs and SAEs similar in frequency across soticlestat vs. placebo
- Main TEAEs for soticlestat over placebo are lethargy/somnolence and constipation
- No anticipated monitoring needs

TAEA = Treatment emergent adverse event; SAE = Serious adverse event
Source: Takeda Wave 1 Market Opportunity Presentation. April 6, 2021

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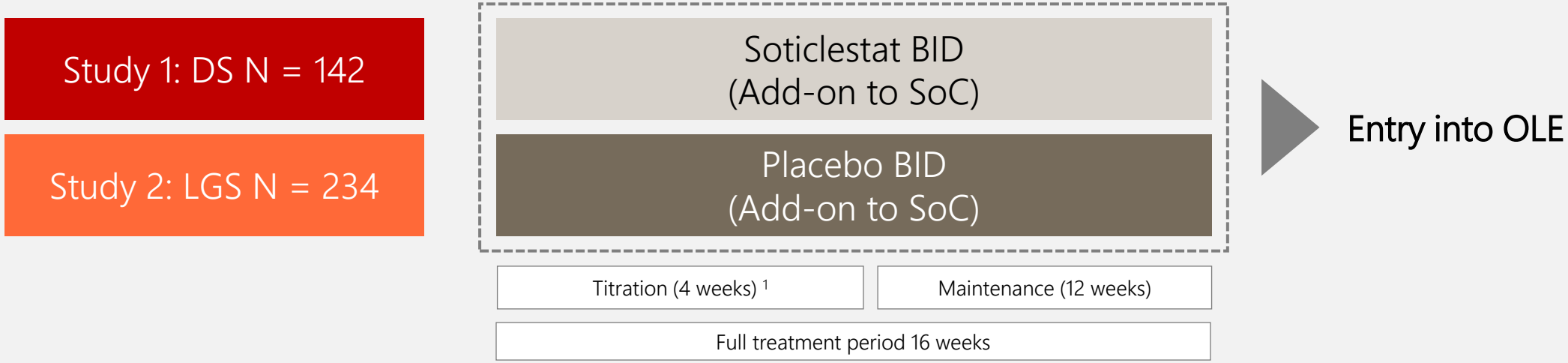
Phase 3 placebo-controlled studies in DS & LGS

Trials being conducted by Takeda

soticlestat



TRIAL DESIGN

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

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

100 mg BID, 200 mg BID, 300 mg BID (mg/kg dosing)
Source: Clinical Trials.gov Accessed October 26, 2021.

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Soticlestat agreement with Takeda holds value of up to $856M[1], creating an expected non-dilutive cash stream

soticlestat

Invested ~$26M upfront & $57M in clinical development

2021	2025*	Est. 2025 and later
Upfront payment • All Ovid financial obligations for soticlestat are terminated	Expected regulatory milestone decision • Takeda funding comprehensive LGS and Dravet trials • Soticlestat is a Wave 1 pipeline priority for Takeda[2]	Commercial milestones & royalties • Tiered double-digit royalties on ALL indications • Up to 20% on GLOBAL soticlestat sales
$196M (Q1'21)	**Up to $650M in additional milestones* + Royalties (up to 20%)** *Potential for combined regulatory and commercial milestone payments	

ROYALTY & MILESTONES TO FUND PIPELINE & BUSINESS DEVELOPMENT

*Based upon (i) estimated primary completion of two, pivotal Phase 3 trials by March 2024, as disclosed by Takeda in materials in July 2022. Takeda disclosed that it anticipates regulatory filings in its fiscal year 2024.

[1] $856M includes the $196M already received as an upfront payment in 1H 2021

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OVERVIEW:

OV329

A potential anti-seizure medicine for rare adult & pediatric epilepsy disorders

A potent, next-generation GABA-aminotransferase inhibitor

6 preclinical models demonstrate anti-seizure activity

- Drug-resistant animal models

Multiple possible applications:

- Focal seizures
- Tuberous sclerosis complex seizures
- Infantile spasms

Safety profiles established in mice, rat and canine models:

- At predicted therapeutic levels, no reported:
  - Genotoxicity, CV effect, adverse CNS effect
- In preclinical studies, potentially better ocular safety margin than vigabatrin

Toxicology & pharmacology supportive of IND filing

Anticipated IND submission and Phase 1 initiation in H2 2022

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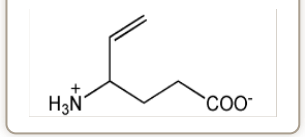
OV329 is a highly potent GABA-aminotransferase inhibitor

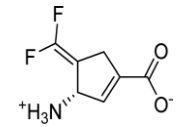
OPPORTUNITY: **Designed to be a potential best-in-class GABA-AT inhibitor based on a validated mechanism with an enhanced benefit/risk profile for epilepsies**

- Engages well characterized target
- More potent than vigabatrin
- Potentially improved safety profile
- Anticipated lower dosing than vigabatrin

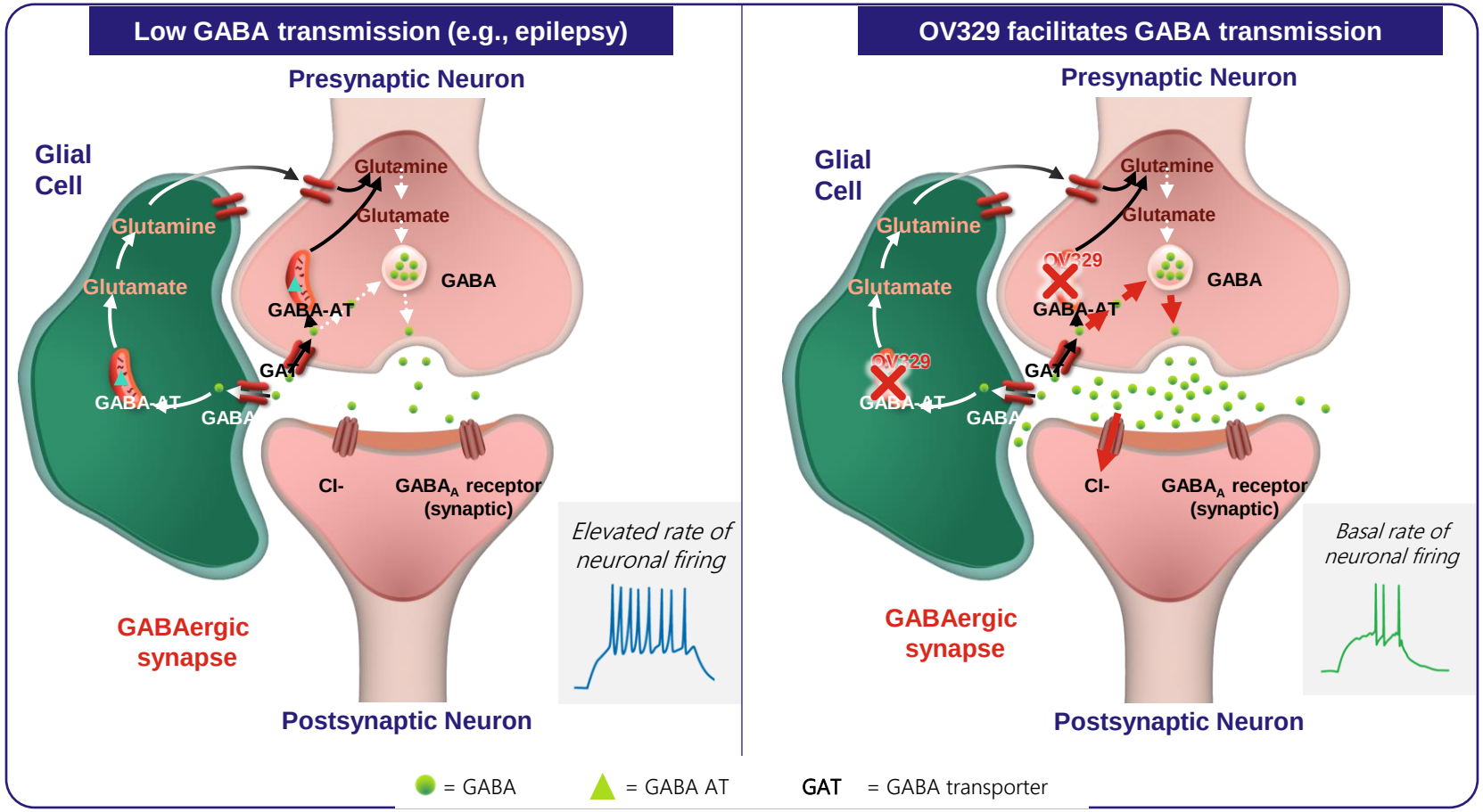
Vigabatrin



OV329



SOURCE:
J Med Chem. 2012 Jan 26; 55(2): 567–575
J Am Chem Soc. 2018 Feb 14; 140(6): 2151–2164
J. Tsai, EILAT 2023 presentation



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Six preclinical models reaffirm OV329 seizure reduction activity, including resistant seizure models[1]

	6 Hz Electrical Stimulation	Maximal Electroshock (MES)	i.v. Pentylenetetrazol (ivPTZ)	NMDA-Induced Infantile Spasm Model	Audiogenic Seizure	Amygdala Kindled	Corneal Kindled	Intrahippocampal Kainate Model of Mesial-Temporal Lobe Epilepsy (MTLE)
Injury Model	Acute/seizure	Acute/seizure	Acute/seizure	Acute/seizure	Acute	Chronic/epilepsy	Chronic/epilepsy	Chronic/epilepsy
Clinical Correlate	Acute focal to bilateral tonic-clonic seizure	Generalized tonic-clonic seizure	Nonconvulsive seizures (eg absence, myoclonic)	Infantile spasms	Generalized seizures	Chronic focal to bilateral tonic-clonic seizure/ Pharmacoresistant seizures	Chronic focal to bilateral tonic-clonic seizure	Mesial temporal lobe epilepsy/ Pharmacoresistant seizures
Species	Mouse	Mouse	Rat	Mouse	Mouse	Rat	Mouse	Mouse
Dosing	Acute (0.01, 0.1, 0.3, 1 mg/kg/day, p.o.)	Acute (1, 3, 10, 30 mg/kg, p.o.)	Acute (5, 20, 40 mg/kg i.p.)	Acute (0.0025, 0.01, 0.1, 1 mg/kg, p.o.)	Acute (0.01, 0.05, 0.1 mg/kg, p.o.)	Acute (30, 40 mg/kg, i.p.)	Acute (1, 3, 10, 20, 30, 40, 60 mg/kg, p.o.)	Acute, single dose (0.01, 0.1, 1, 10 mg/kg, p.o.; 10 mg/kg, i.p.) Subacute (8 days q.d.) 0.3, 1.0 and 3.0 mg/kg/day (p.o.)
Activity	—	—	+	+	+	+	+	+

1. Ovid data on file

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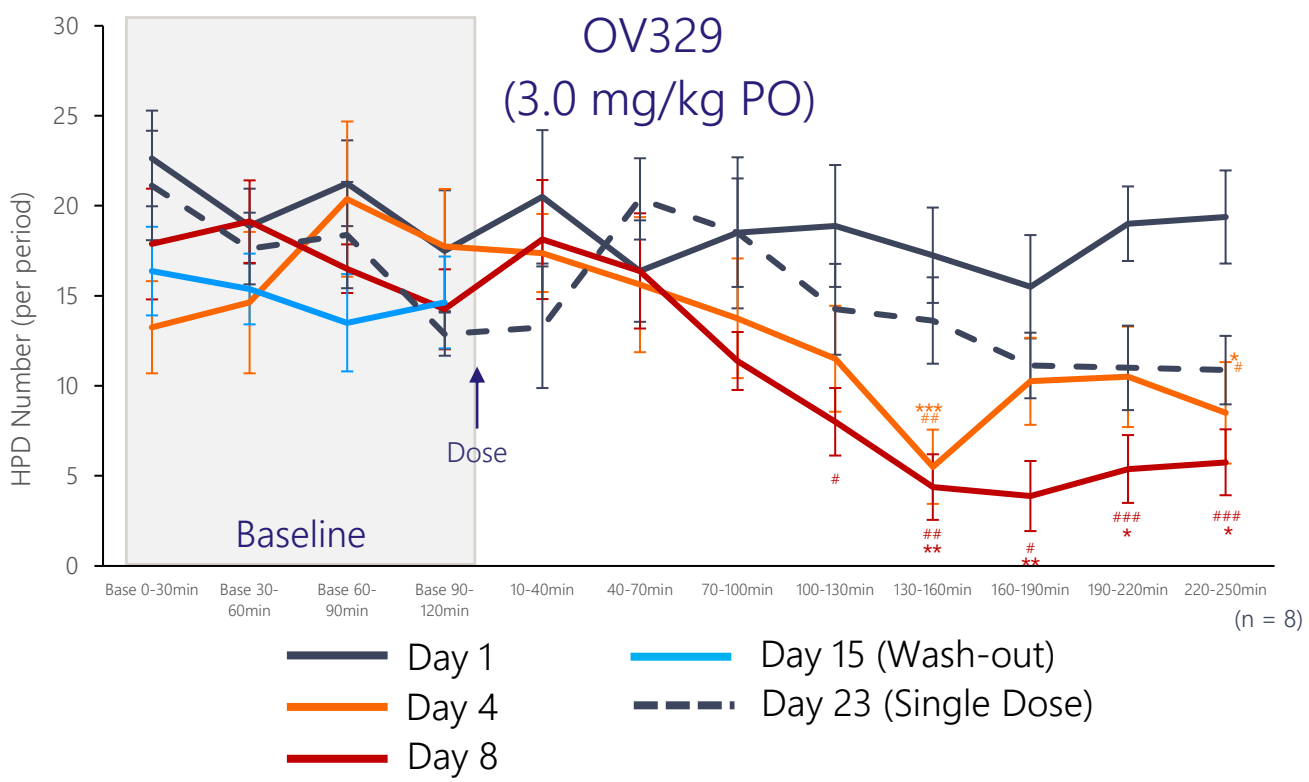
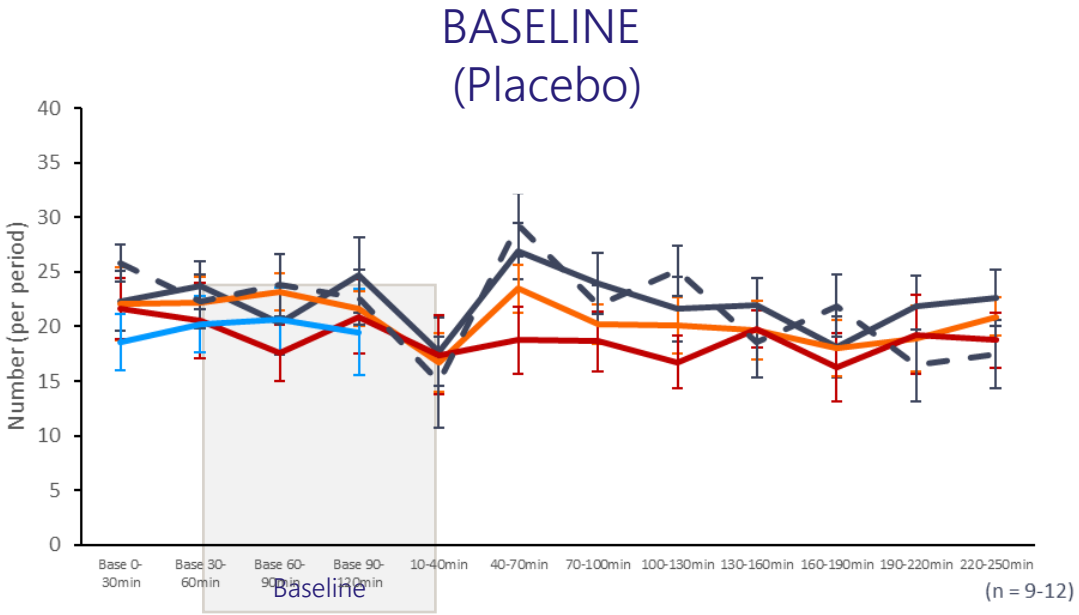
Daily dosing (3 mg/kg) significantly reduced number of focal seizures in MTLE model





Data are expressed as mean ± SEM. *,**: p < 0.05, 0.01 vs Baseline; #, ##:p < 0.05, 0.01 vs Day 1

3.0 mg/kg in mice reduced seizures (HPD) by ~70% compared to baseline levels at Day 8

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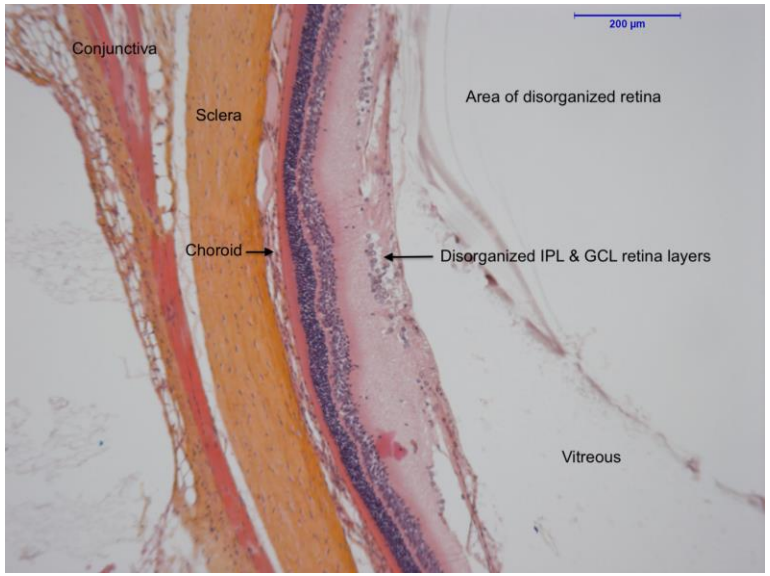
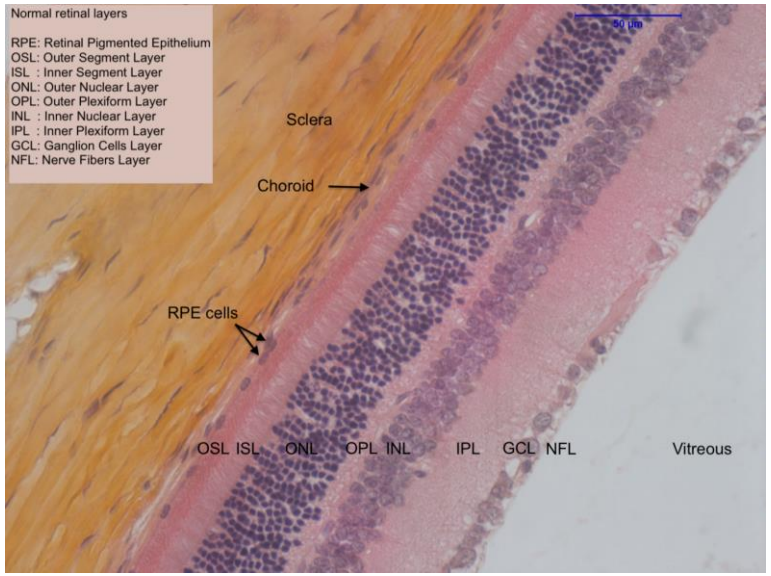
No ocular effects seen following chronic exposure with OV329 (3 mg/kg)

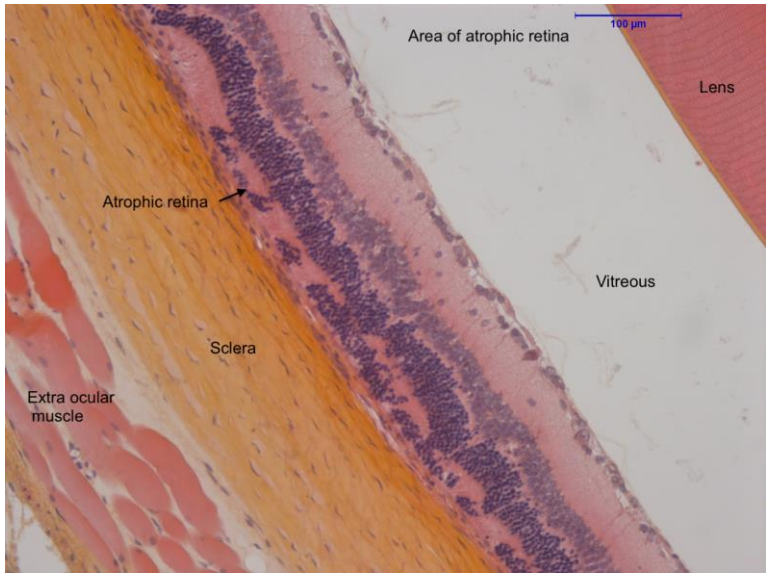
Vehicle



OV329 3.0 mg/kg



Vigabatrin 300 mg/kg



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

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

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OVID, *Data on file*

OVERVIEW:

OV350 & KCC2 direct activators

Library of potential first-in-class direct activators of the KCC2 transporter

Innovative KCC2 activator program in industry

- Consulting support by neuropharmacologist, Prof. Steve Moss
- Chemistry & lead identification conducted by AstraZeneca[1]

Franchise in a program

- OV350 & compound library
- Individual compounds potentially suitable for:
  - IV – acute indications
  - Oral – chronic needs

Novel mechanism of action

- Only known direct KCC2 activator
- Measurable with biomarker (EEG high gamma power spectrum)[2]

Broad therapeutic potential in rare & common populations

- Genetic epilepsies
- Acute epilepsies
- Neuropathic pain
- Behavioral & cognitive conditions

Does not induce sedation[2]

in preclinical models

Preclinical POC demonstrated in-vivo & in-vitro in resistant seizures and other CNS indications[3]

1. $12.5M is comprised of $5M cash payment and $7.5M Ovid stock; royalties are single digit up to 10% on net sales 2. Maguire J. and Moss S.J. (in preparation) 3. Ovid data on file.

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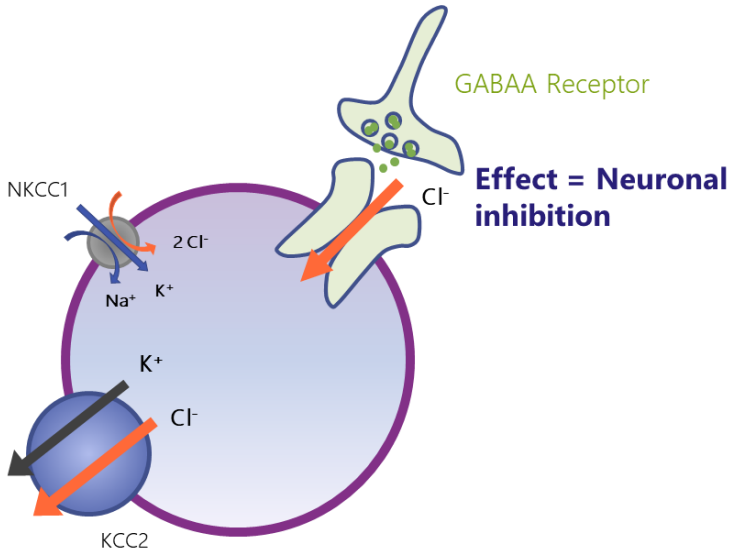
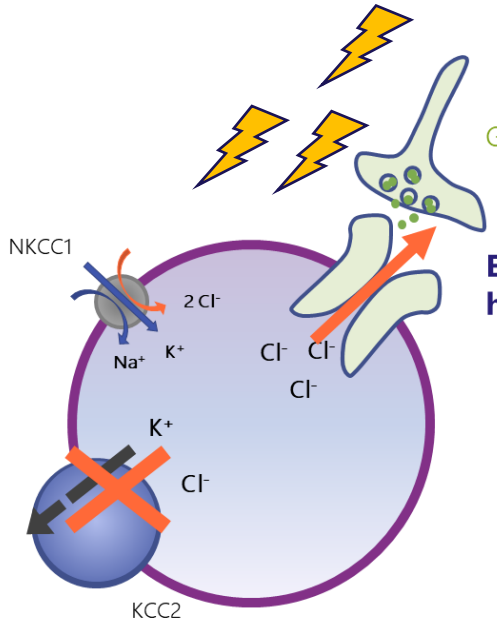
KCC2 transporter is central to regulating neuronal inhibition, reducing seizures[1]

Healthy Neuron



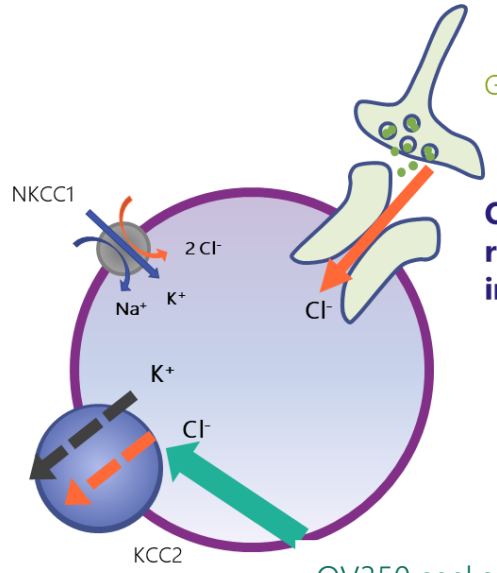
Effect = Neuronal inhibition

Epileptic Neuron



Effect = Neuronal hyperexcitability

Potential Effect of OV350



OV350 thought to return neuron to inhibitory state

OV350 seeks to directly activate the KCC2 transporter to improve chloride extrusion, thereby reversing neuronal hyperexcitability that produces seizures

[1] 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

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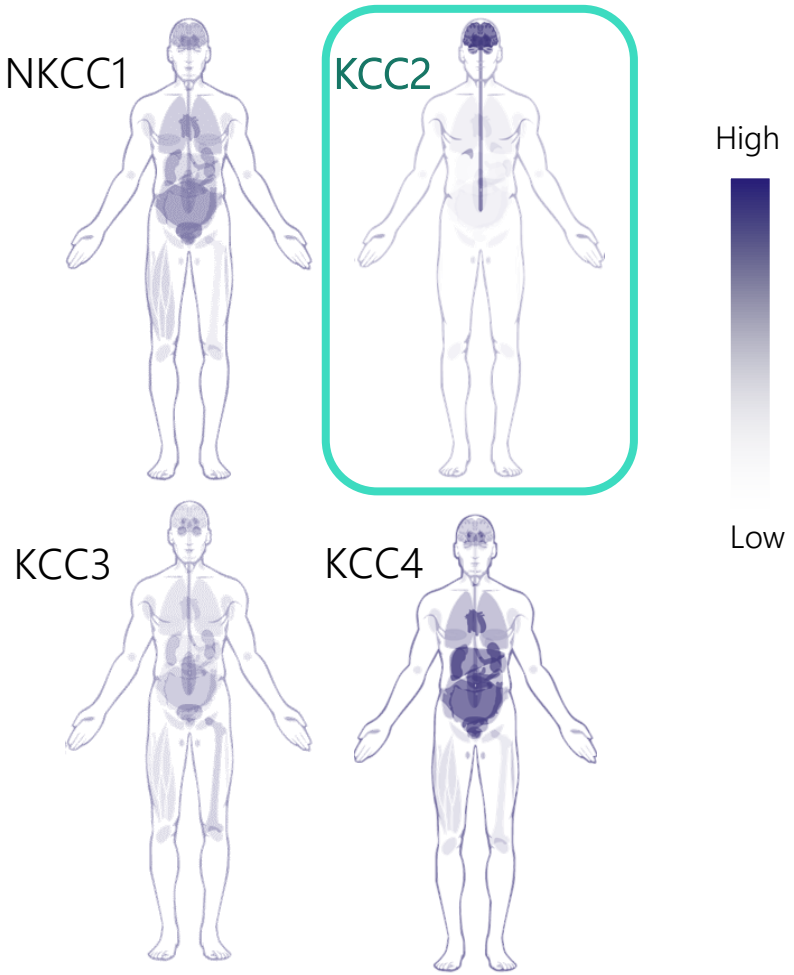
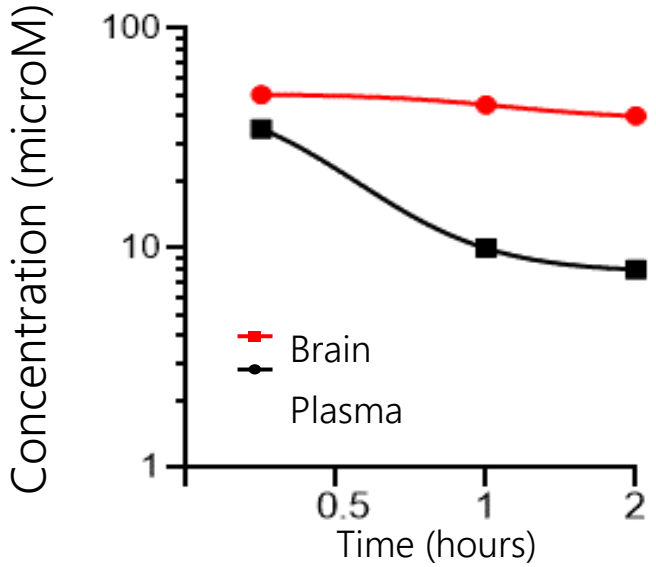
OV350 preclinical models show rapid, stable accumulation in the brain with a translatable pharmacodynamic biomarker[1]

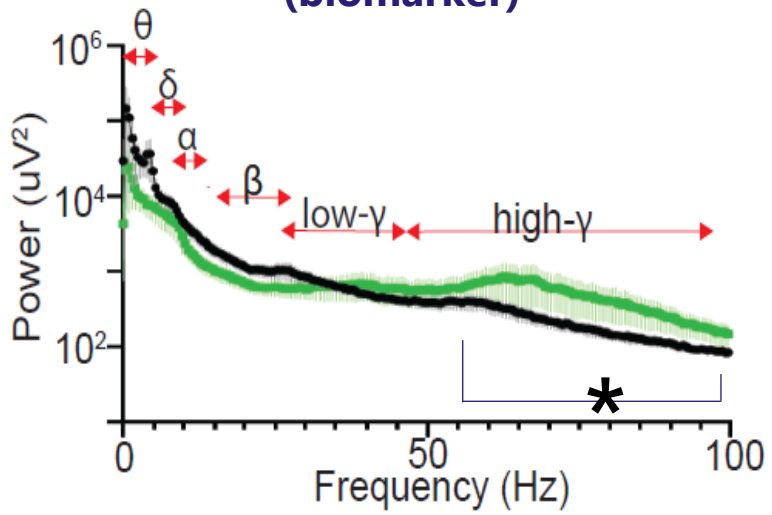
KCC2 is expressed exclusively in neurons, unlike other K/Cl co-transporters



OV350 rapidly accumulates in rodent brain via IV/IP dosing



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

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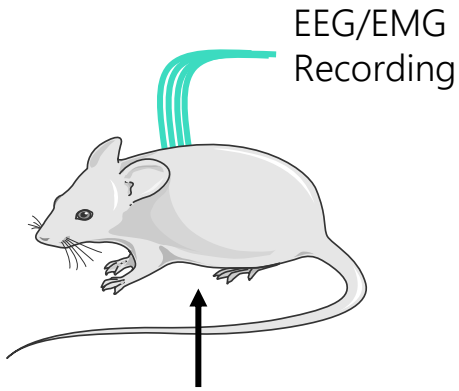
In-vivo studies demonstrate mechanistic proof of concept

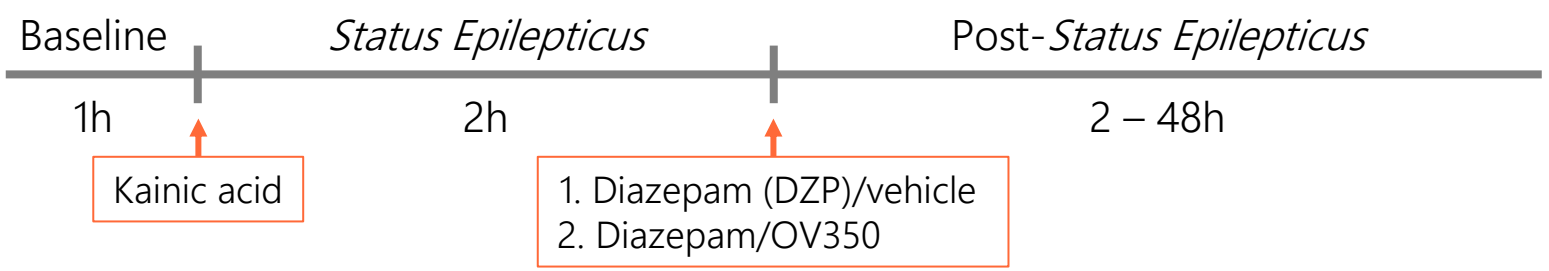
OV350 restores the efficacy of diazepam to terminate "refractory" *Status Epilepticus* in preclinical study

Adult Mouse

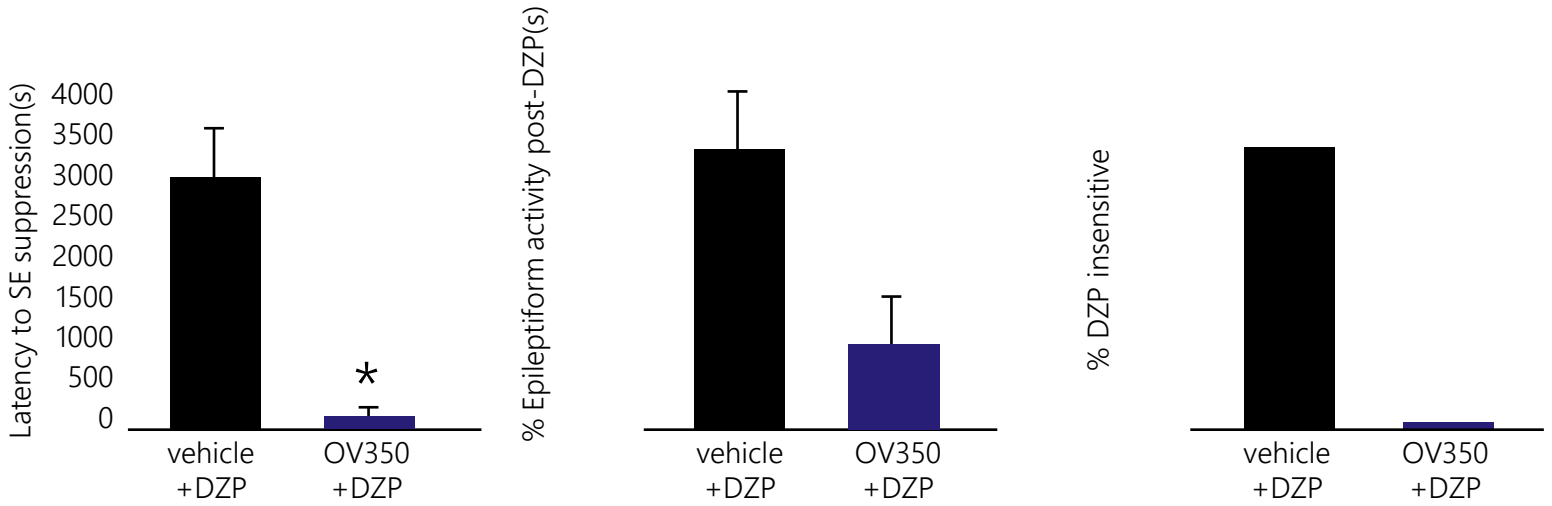


- Potentiating KCC2 activity observed to be well tolerated in-vivo
- Unlike other anti-convulsants, OV350 appears to not induce sedation

Experimental design



Post-treatment EEG analysis



*p<0.05 by academic lab t-test

Source: Maguire J. and Moss S.J. (in preparation)

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Transforming through business development

Capital from soticlestat licensing deal, coupled with expertise and access, allows for pursuit of successive disciplined and targeted transactions

Transaction Goals

- Leverage institutional epilepsy expertise
- Complement and enhance current pipeline
- Secure next-generation discovery platforms
- Ensure access to key drug delivery technologies for the CNS

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Investment highlights

+ Strong balance sheet

$152.4M — in cash, cash equivalents and marketable securities[1]

70.4M — shares of common stock outstanding[2]

Potential non-dilutive cash stream from Takeda's development and commercialization of soticlestat

+ Veteran team

with a track record of developing and commercializing blockbuster medicines

+ Investing in our pipeline and people today to conquer epilepsies and brain disorders tomorrow

+ Epilepsy franchise

- 2 small molecule programs
- Potential 1st-in-class or best-in-class medicines
- Novel, complementary mechanisms of action for the potential treatment of epilepsy & seizures
- Despite available antiepileptic drugs, there is a significant unmet need

+ Genetic seizure programs

- Investigational medicines for genetic seizure-related disorders
- Applying proven platforms
- Harnessing accelerated, replicable development approach

+ Pursuing transformative business development

1 As of 6/30/22
2 As of 6/30/22, on an as if converted basis

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Ovid™ Therapeutics

Conquer epilepsies & brain disorders with courageous science















Appendix

SCIENTIFIC ADVISORS

Biotech company creators; world-leading epileptologists



Robert Langer, Sc.D.
Chairman , Scientific & Clinical Advisory Board



Jackie French, M.D.,
Scientific & Clinical Advisory Board



Bruce Sullenger, Ph.D,
Scientific & Clinical Advisory Board



Jan Torlief Pedersen
Advisor



Bernd Schmidt, M.D., Ph.D.
Advisor



Brian Cox
Advisor
Fmr. Head of Chemistry, Novartis

BOARD OF DIRECTORS

Career-long experts in CNS & genetic platforms



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Director, founder in Neumora, Gates Fdn., Wyeth, AZ, Pfizer



Kevin Fitzgerald, Ph.D.
Director, Alnylam Head of Research



Karen Bernstein, Ph.D.
Founder & Chairman Biocentury



Barbara Duncan MBA
Fmr. CEO DOV Therapeutics; Fmr. CFO Intercept



Bart Friedman, J.D.
Fmr. partner Cahill Gordon & Reindel LLP; Fmr. SEC

UNDERPINED BY EXPERT CNS ENGINE

ACADEMIC COLLABORATOR

Tufts UNIVERSITY | School of Medicine

Moss Labs for Basic & Translational Neuroscience Research



- Rich library of data allows for rapid comparative modeling
- Wet lab, sterile cell culture room and vivarium
- Screening tools & assays
- Full high-throughput electrophysiology suite (qEEG)

GENETIC MEDICINES ENGINE

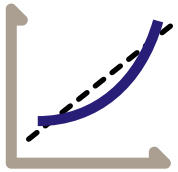
COLUMBIA

Chung Labs of Human Genetics & Precision Medicine



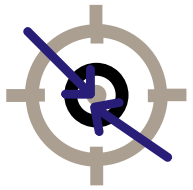
- Library of targets, PSCLs & animal models
- Natural history and pathology mapping for rare CNS disorders
- A NORD rare disease center of excellence
- “Trial ready” community toolbox

Approach to CNS development



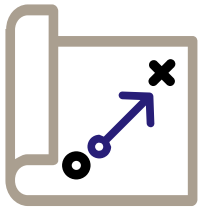
SENTINEL STRATEGY

Aim to demonstrate impact in rare, treatment-resistant epilepsies, then expand to more common epilepsies and CNS pathologies



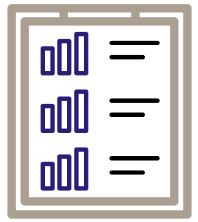
PIPELINE OF UNIQUE & COMPLEMENTARY MECHANISMS

Seek biological targets implicated in seizures with a pipeline of differentiated and potentially complementary mechanisms



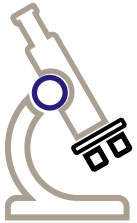
FAST-TO-PATIENT PLAYBOOK

Seek efficient development with homogeneous communities who are trial-ready in conditions with well-characterized disease pathology & progression



MEASUREABLE ENDPOINTS

Pursue conditions with identifiable & quantifiable seizures that support measurement in clinical trials (such as via EEG)



DE-RISK CLINICAL DEVELOPMENT

Endeavor to develop “best-in-class” medicines for known targets and leverage proven modalities for “first-in-class” targets

Harness panels of translatable animal models & iPSCLs* screening in preclinical development confirm activity

Small, signal confirming trials show target engagement confirmation & effect in Phase 1

*induced pluripotent stem cells

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