Ovid Therapeutics

Corporate Overview

(NASDAQ: OVID)

©2022 OVID THERAPEUTICS INC. | ALL RIGHTS RESERVED

MAY 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; 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.

The trademarks included in this presentation are the property of the owners thereof and are used for reference purposes only.

©2022 OVID THERAPEUTICS INC. | ALL RIGHTS RESERVED

Overview: Ovid Therapeutics

+ Strong balance sheet

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

70.4M shares of outstanding

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

+ Striving to conquer epilepsies & brain disorders with courageous science

+ 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

+ 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 6/01/22

©2022 OVID THERAPEUTICS INC. | ALL RIGHTS RESERVED

Epilepsy by the numbers



~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

Medicines with new mechanisms and improved tolerability are needed for patients who continue to experience refractory seizures

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)

©2022 OVID THERAPEUTICS INC. | ALL RIGHTS RESERVED

Our development strategy

Criteria across targeted genetic & small molecule epilepsy candidates

- Potential 1st-in-class or best-in-class therapeutics
- Blood-brain barrier penetration
- Mechanistically designed to target
- Hard endpoints
- "Sentinel" indication strategy to establish clinical impact & expand
- Tolerability & safety
- Accelerate development (trial ready communities, direct to patient trials)

©2022 OVID THERAPEUTICS INC. | ALL RIGHTS RESERVED

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					• Regulatory milestones • Sales milestones • Royalties
OV329 GABA aminotransferase inhibitor	Tuberous Sclerosis Complex, Infantile Spasms and Focal Seizures					Anticipated IND in 2022
OV350 KCC2 transporter activator licensed from: AstraZeneca	Resistant epilepsies and other neuro-pathologies					

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

©2022 OVID THERAPEUTICS INC. | ALL RIGHTS RESERVED

Franchise of potential, novel epilepsy medicines

Supported by the Ovid team that led soticlestat's development

IN-LICENSED

OV329

Northwestern University

Potential next generation oral GABA aminotransferase inhibitor with an enhanced benefit/risk profile and administration in pre-clinical development for tuberous sclerosis and infantile spasms

IN-LICENSED

OV350

AstraZeneca

Lead compound and 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 received upfront[1])

[1] In 1H 2021

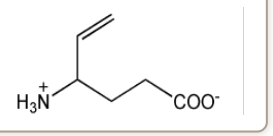
©2022 OVID THERAPEUTICS INC. | ALL RIGHTS RESERVED

OV329 is a highly potent GABA aminotransferase inhibitor

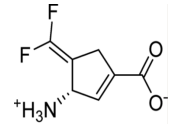
OPPORTUNITY: **Designed to be potential best-in-class therapeutic based on a validated mechanism with an enhanced benefit/risk profile for epilepsies**

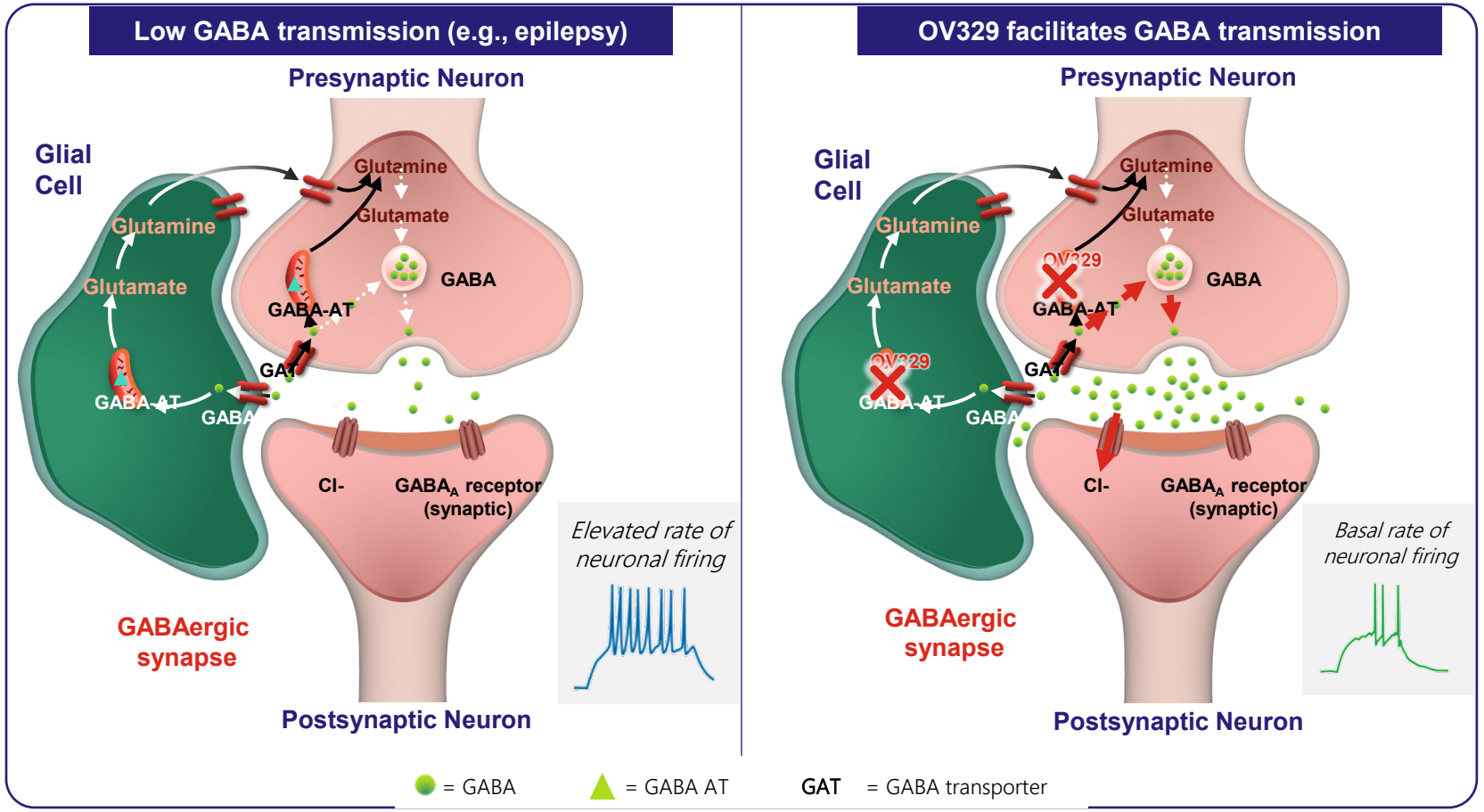
- Well-characterized target
- Similar mechanism of action to vigabatrin
- Potentially more potent than vigabatrin
- Potentially improved safety profile

Vigabatrin



OV329

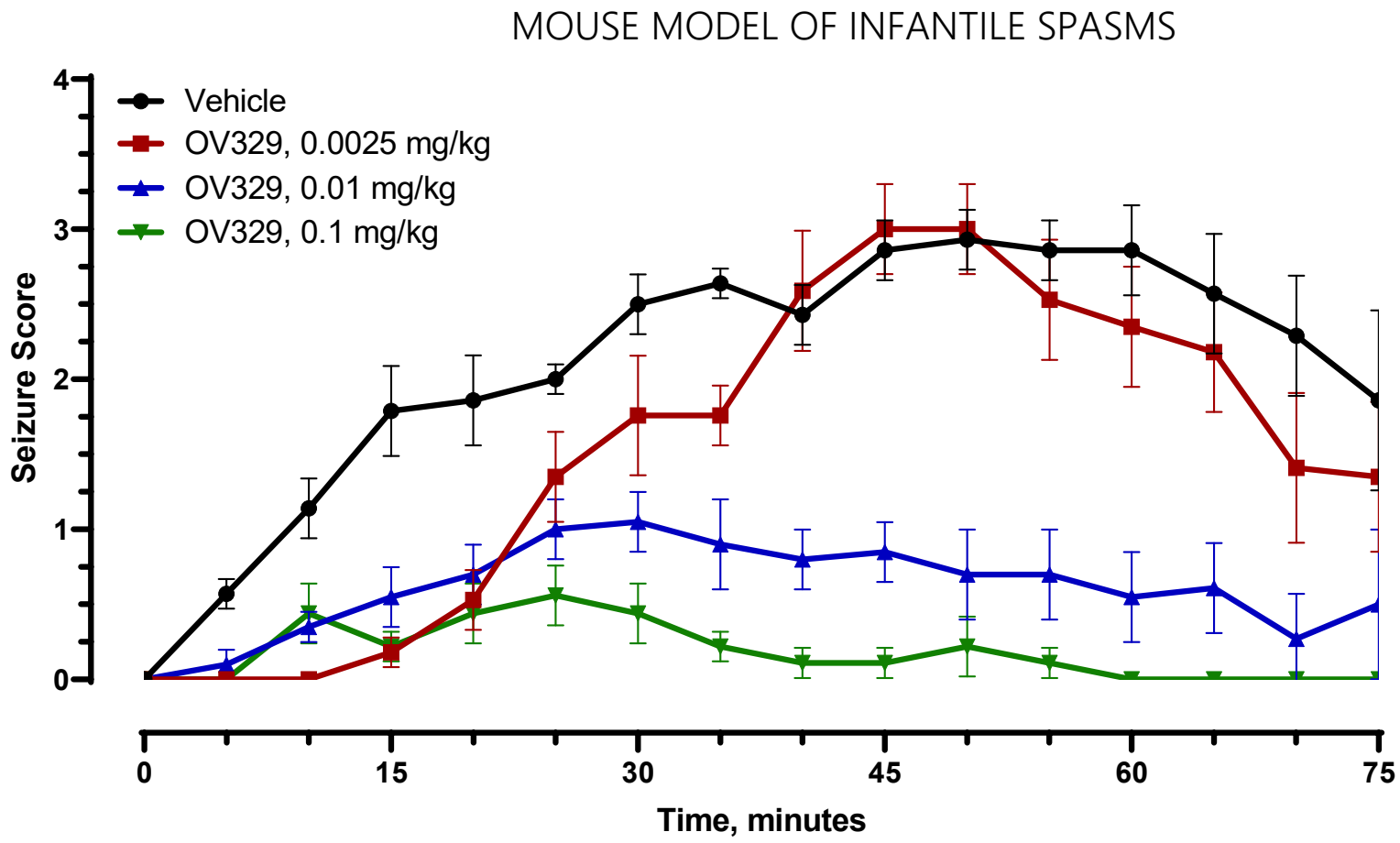




SOURCE:
J Med Chem. 2012 Jan 26; 55(2): 567–575
J Am Chem Soc. 2018 Feb 14; 140(6): 2151–2164

©2022 OVID THERAPEUTICS INC. | ALL RIGHTS RESERVED

OV329 is active in models of drug resistant seizures
Demonstrates potential pharmacologic activities at a single dose

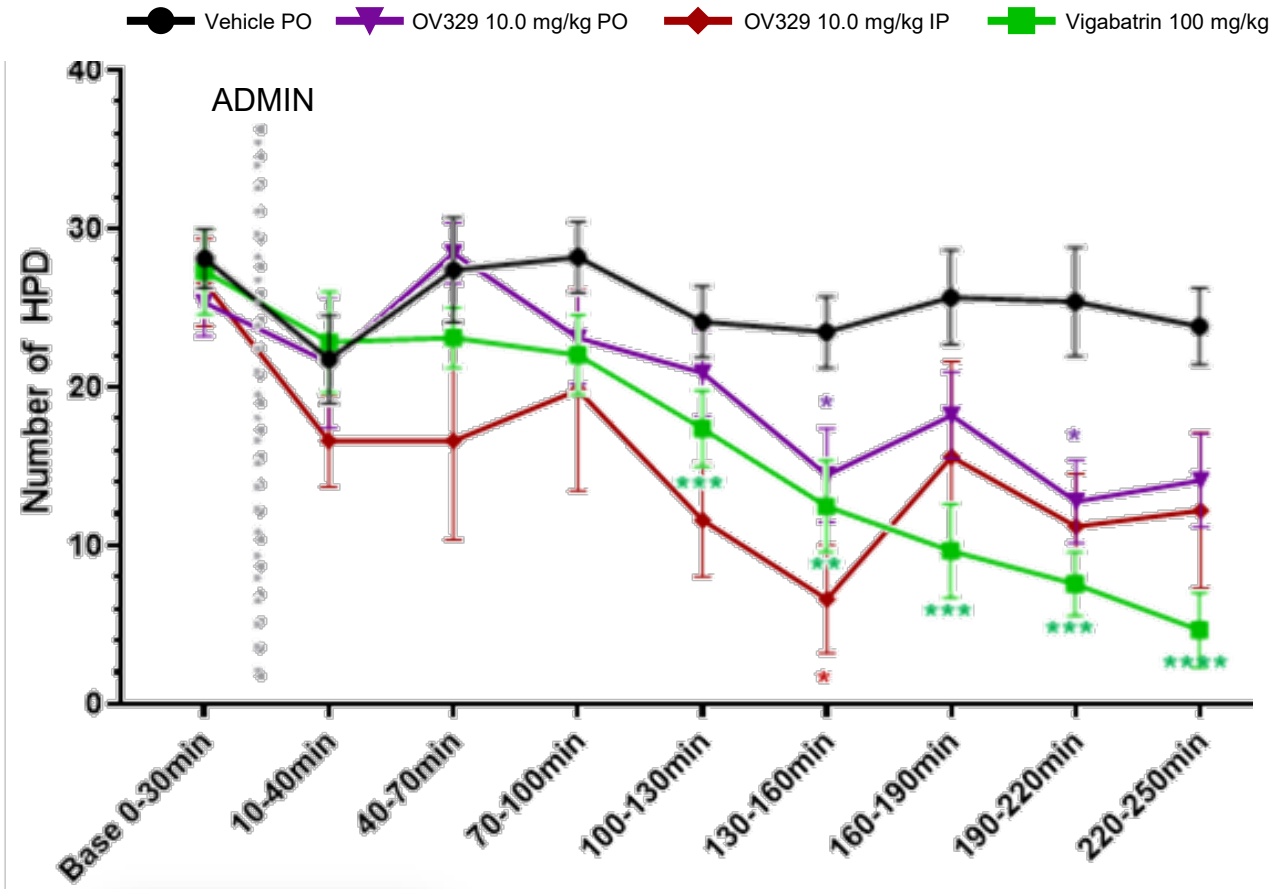


Acute NMDA-Induced Injury
Model described by Shi *et al.*, 2014 (PMID 26600368)
Performed by Paul Davies, Tufts University

Source: Ovid Therapeutics internal models

©2022 OVID THERAPEUTICS INC. | ALL RIGHTS RESERVED

Mesial-temporal lobe epilepsy mouse model of drug resistant epilepsy



- OV329 achieved a 55% reduction in seizure activity after intraperitoneal administration
- OV329 achieved a 46% reduction after oral administration

Data are expressed as mean ± SEM. *,**, ***, ****: p < 0.05, 0.01, 0.001 or 0.0001

Results

Suggest OV329 significantly suppressed the number of focal seizures in the MTLE mouse model at 10mg/kg.

[1]Duveau, et al. *CNS Neurosci Ther.* 2016;22(6):497-506;
[2]Sarmiere, PD et al. *American Epilepsy Society Meeting*, 2021

©2022 OVID THERAPEUTICS INC. | ALL RIGHTS RESERVED

OV350 overview

Potential novel direct activator of the KCC2 transporter

OPPORTUNITY: **Therapies that directly activate KCC2 target implicated in epilepsies and other CNS pathologies**

Library of KCC2 activators, including lead compound

- Pre-clinical proof of concept demonstrated in-vivo and in-vitro in resistant seizures

Deep unmet need

- 1/3 - 1/2 of all people with epilepsies continue to experience seizures[2,3,4]

In-licensed from AstraZeneca

- Similar to value-creating transaction with soticlestat
- $12.5M upfront and milestones for: $8M in clinical development; $45M in approval; up to $150M in commercial milestones & royalties[1]

Recognized academic collaborators

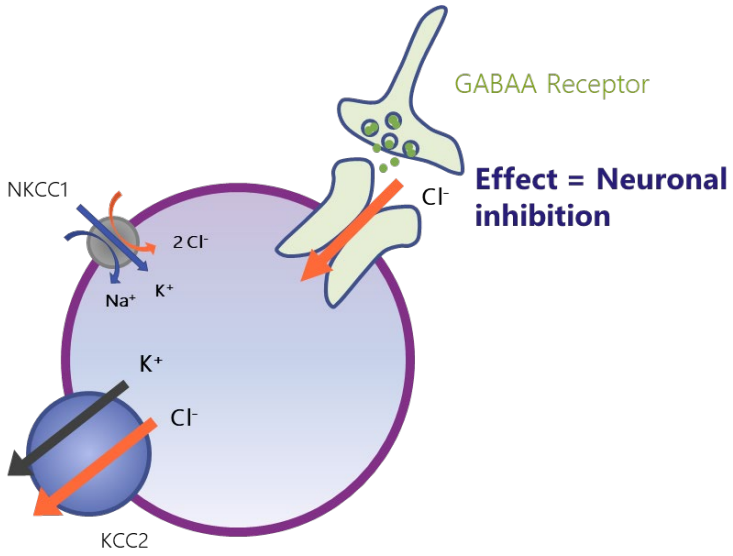
- Drs. Steve Moss of the Tufts Lab for Translational Neuroscience, Jamie Maguire & Aaron Goldman add expertise in neuropharmacology

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. Kwan, P., and Brodie, M. J. (2000). Early identification of refractory epilepsy. *N. Engl. J. Med.* 342, 314–319.; 3. Shorvon, S., and Luciano, A. L. (2007). Prognosis of chronic and newly diagnosed epilepsy: revisiting temporal aspects. *Curr. Opin. Neurol.* 20, 208–212.; 4. Cascino, G. D. (2008). When drugs and surgery don't work. *Epilepsia* 49, 79–84.

©2022 OVID THERAPEUTICS INC. | ALL RIGHTS RESERVED

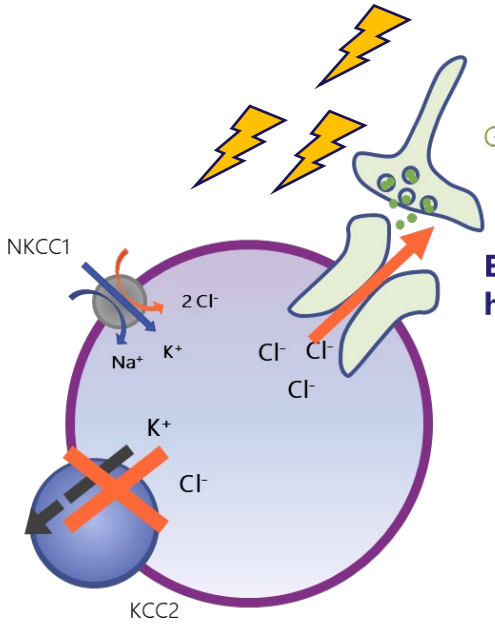
KCC2 transporter is central to regulating neuronal inhibition; reducing seizures[1]

Healthy Neuron



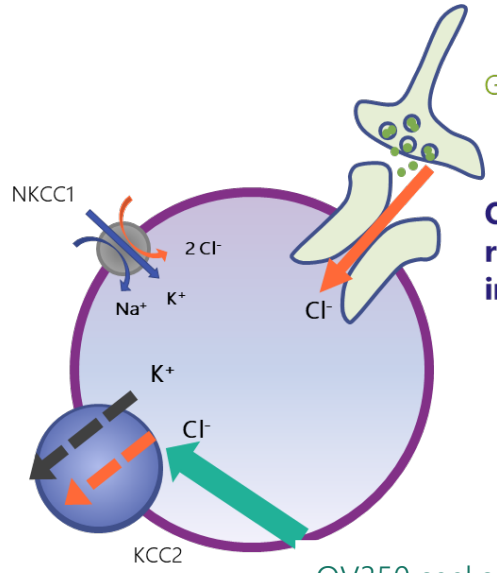
Effect = Neuronal inhibition

Epileptic Neuron



Effect = Neuronal hyperexcitability

Potential Effect of OV350



OV350 thought to return neuron to inhibitory state

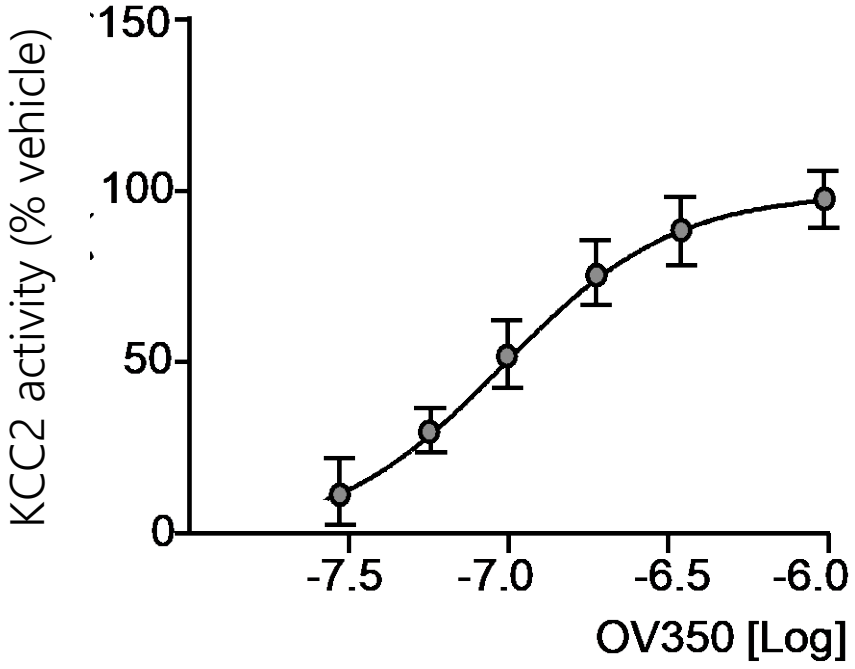
OV350 seeks to directly active the KCC2 transporter to improve chloride extrusion, thereby reversing neuronal hyperexcitability that produces seizures

[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

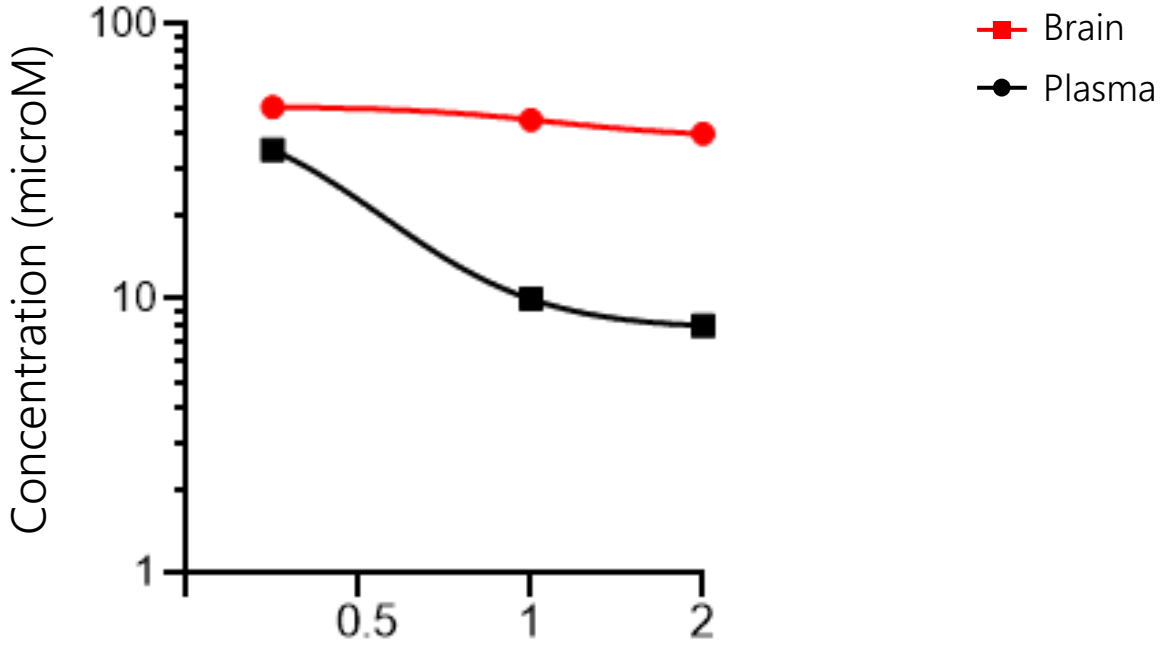
©2022 OVID THERAPEUTICS INC. | ALL RIGHTS RESERVED

OV350 pre-clinical models show rapid brain penetration; stable accumulation

OV350 directly potentiates KCC2 activity with high affinity



OV350 rapidly accumulates in rodent brain via IV/IP dosing



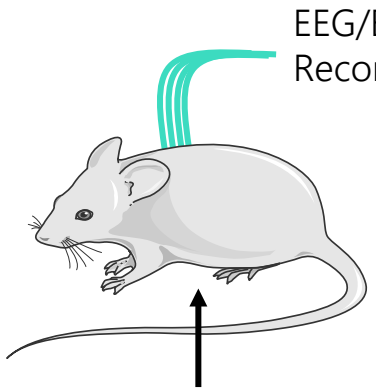
- OV350 directly binds and potently activates KCC2 at **nanomolar** affinity
- OV350 in-vivo pharmacokinetics shows high **micromolar** accumulation in the brain within minutes.

©2022 OVID THERAPEUTICS INC. | ALL RIGHTS RESERVED

In-vivo studies demonstrate mechanistic proof of concept:

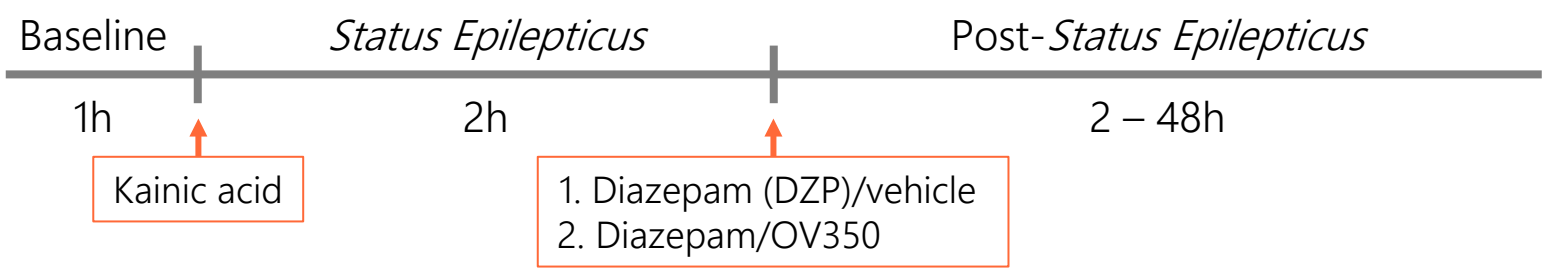
OV350 restores the efficacy of diazepam to terminate "refractory" *Status Epilepticus* in preclinical study

Adult mouse

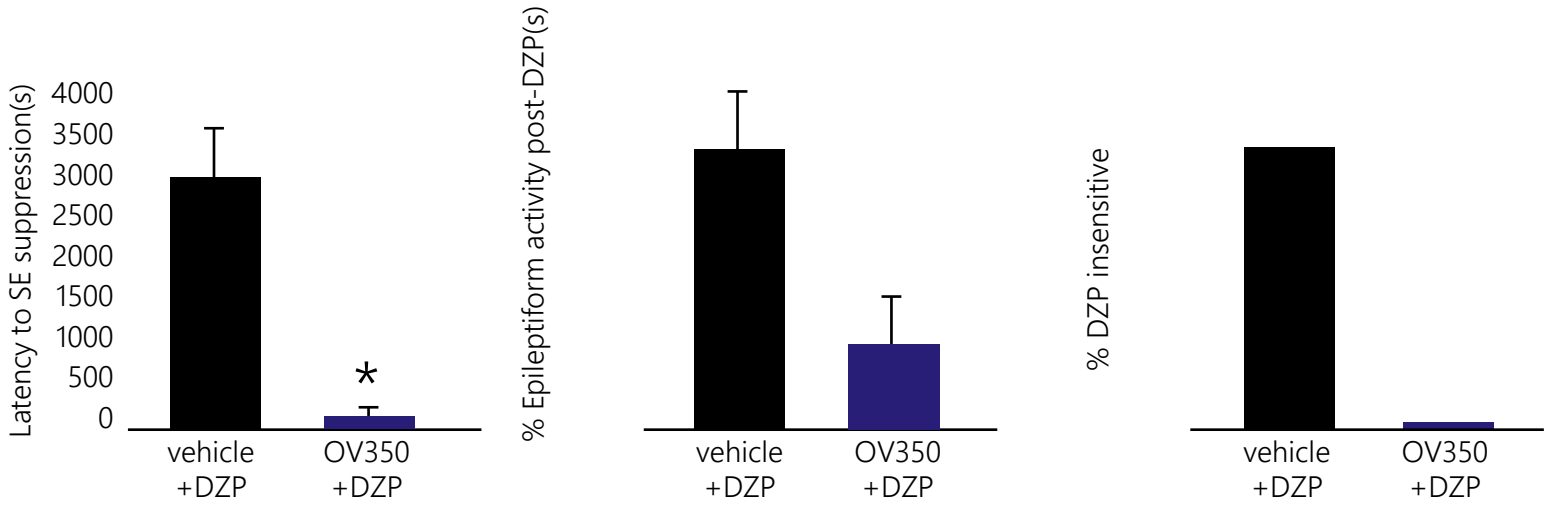


- Potentiating KCC2 activity observed to be well-tolerated in-vivo
- Unlike other anti-convulsants, OV350 appears to not induce sedation

Experimental design



Post-treatment EEG analysis



*p<0.05 by academic lab t-test

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

©2022 OVID THERAPEUTICS INC. | ALL RIGHTS RESERVED

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

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 disclose by Takeda in materials dated May 11, 2022, and (ii) Takeda disclosed on its annual earnings call, held on May 11, 2022, that it anticipates regulatory filings in its fiscal year 2024.

1 $856M includes the $196M already received as an upfront payment in 1H 2021
2 Takeda Pipeline Table, Wave 1 section, https://www.takeda.com/4a21eb/siteassets/system/what-we-do/research-and-development-rd-in-takeda/our-pipeline/qr2021_q1_pipeline_en.pdf Accessed October 26, 2021

©2022 OVID THERAPEUTICS INC. | ALL RIGHTS RESERVED

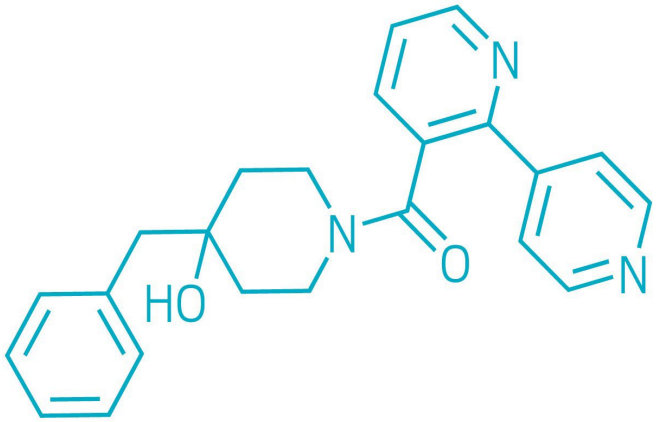
soticlestat overview

Soticlestat offers promise to reduce seizure susceptibility and improve seizure control[1]

SOTICLESTAT OVERVIEW

- Potential to be a first-in-class cholesterol 24-hydroxylase inhibitor in Dravet and Lennox-Gastaut syndromes
- Part of Takeda's Wave 1 CNS pipeline[2]
- Many Dravet & Lennox-Gastaut patients remain refractory[3,4]
- Profile may support early use in treatment paradigm; data does not currently indicate the safety and monitoring challenges associated with other new AEDs[5]
- Identified patient communities (30-50K diagnosed LGS in US; ~10K diagnosed DS in US)[6,7]

WELL-CHARACTERIZED MECHANISM OF ACTION

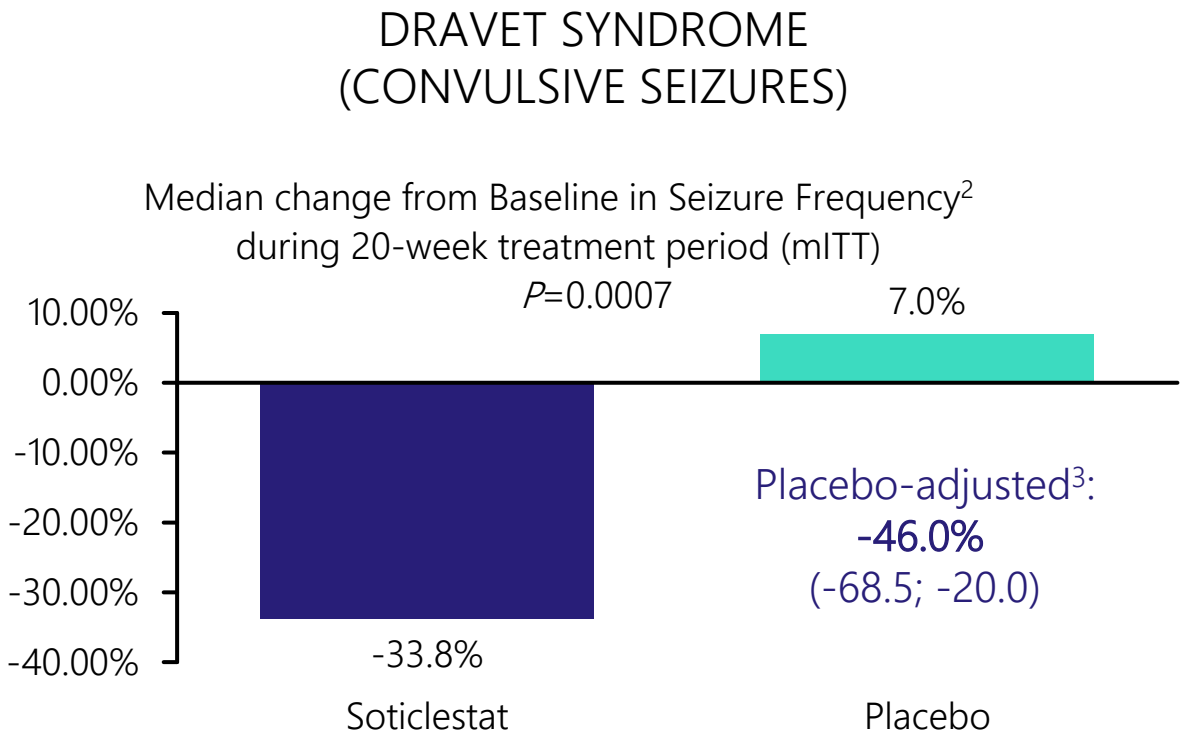


Dose dependent response[8,9]
Reduces glutamatergic signaling & reduced inflammation[8,9]

[1] Salamone A, et al. ECE 2018 [2] Hahn et al. *AES* 2020, [3] Takeda Wave 1 Pipeline Market Opportunity Call Held April 6, 2021. [4] Samanta D. *Neuropediatrics.* 2020 Apr;51(2):135-145. [5] FINTEPLA prescribing information label, pages 5-8. [6] Trevathan E. *Epilepsia.* 1997 Dec;38(12):1283-8. [7] Wu Y. *Pediatrics* 2015;136:1310–5.., [8] Salamone A, et al. ECE 2018., [9] Nishi T, et al. AAN 2018.

©2022 OVID THERAPEUTICS INC. | ALL RIGHTS RESERVED

PHASE 2 ELEKTRA: Soticlestat demonstrated statistically significant seizure reduction in Dravet Syndrome[1]



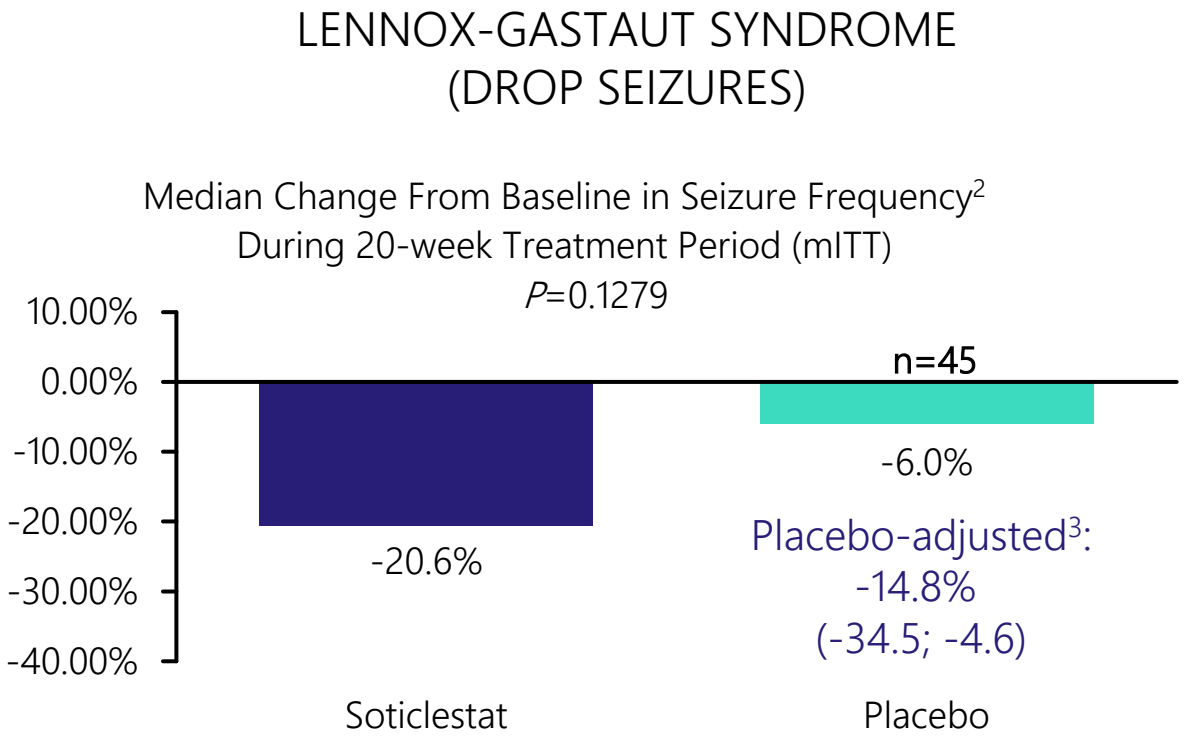
DRAVET SYNDROME
✓ Statistically significant placebo-adjusted median seizure reduction of 46%
✓ DS cohort was not powered for efficacy

[1]Hahn et al. AES 2020; [2]Seizure frequency per 28 days; [3]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.

Source: Takeda Wave 1 Market Opportunity Presentation. April 6, 2021

©2022 OVID THERAPEUTICS INC. | ALL RIGHTS RESERVED

Numeric seizure reduction in Lennox-Gastaut Syndrome[1]



LENNOX-GASTAUT SYNDROME	
✓	Placebo-adjusted median seizure reduction of 14.8% did not reach statistical significance
✓	Impacted by fact that LGS cohort used a broad definition of drop seizure frequency at baseline of 4 to >5,000 drop seizures/28 days
✓	Sensitivity analysis supportive of more stringent, countable drop seizure definition

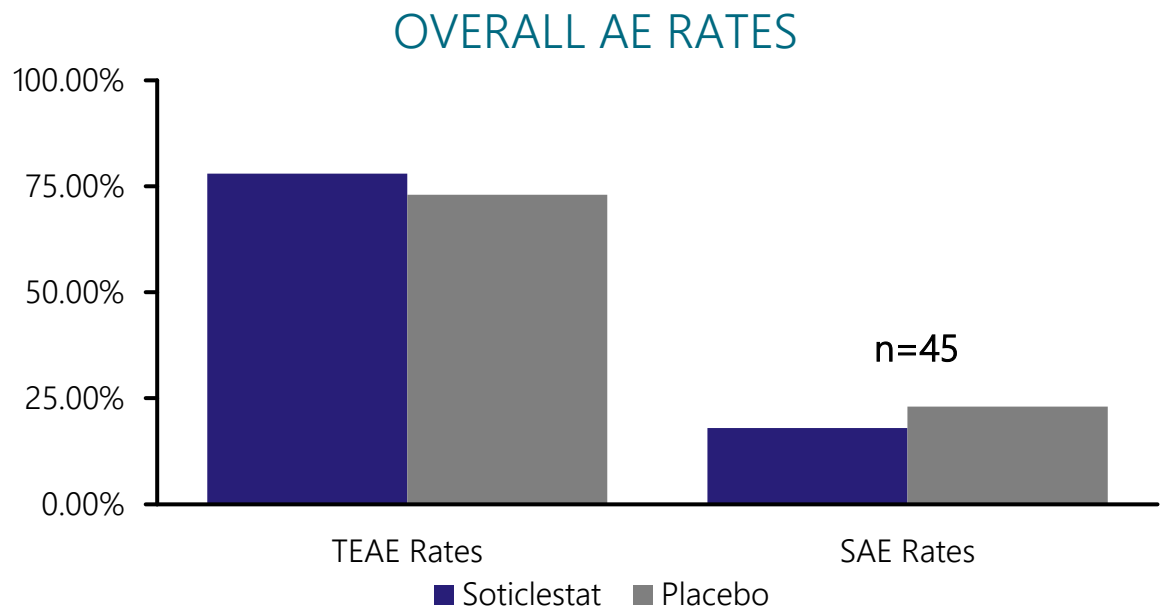
Encouraging efficacy results in LGS support moving into Phase 3 with appropriate sample size and stringent, countable drop seizure definition

1Hahn et al. AES 2020; 2Seizure frequency per 28 days; 3Asymptotic 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.
Source: Takeda Wave 1 Market Opportunity Presentation. April 6, 2021

Ovid Therapeutics
©2022 OVID THERAPEUTICS INC. | ALL RIGHTS RESERVED

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

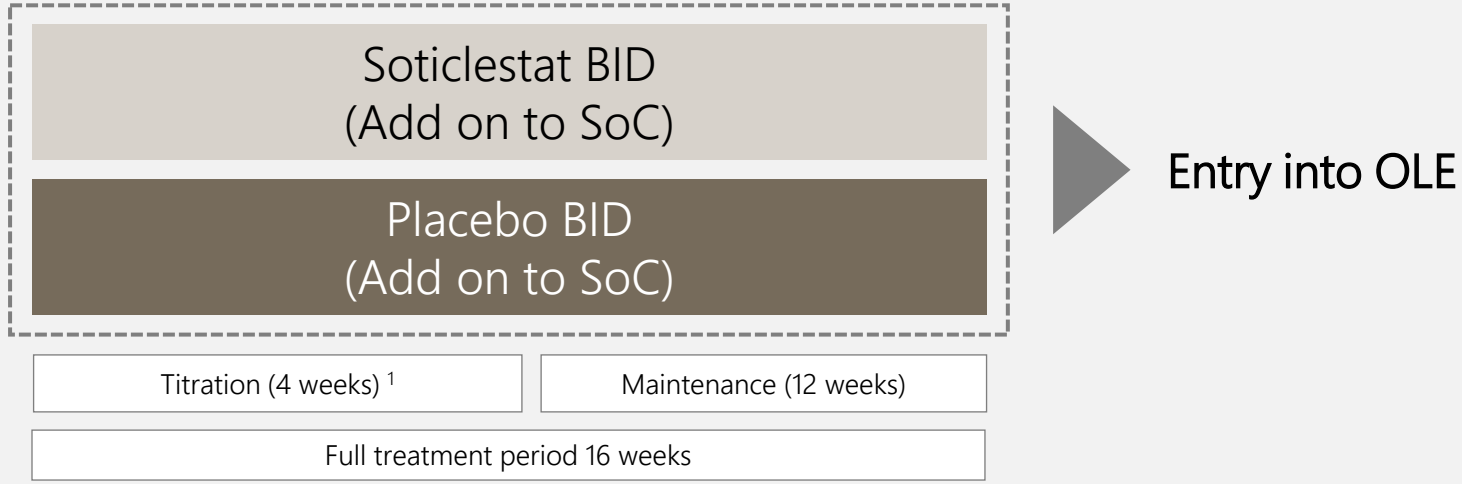
©2022 OVID THERAPEUTICS INC. | ALL RIGHTS RESERVED

Phase 3 Placebo-controlled studies in DS & LGS

Trials being conducted by Takeda

Study 1: DS N = 142

Study 2: LGS N =234



TRIAL DESIGN

- Trial design based on feedback from FDA, EMA & PMDA
- Ages ≥ 2 years
- Adjunctive to AEDs
- 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.

©2022 OVID THERAPEUTICS INC. | ALL RIGHTS RESERVED

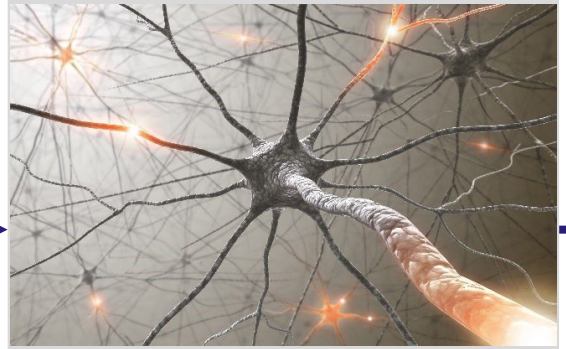
Columbia collaboration is a research engine that enables a replicable approach for discovering & translating genetic epilepsy targets

Discovery & research collaboration with Columbia University



Library of targets, PSCLs & animal models

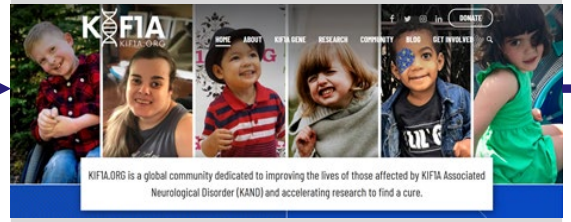
Screening Tools



Screening tools & assays help demonstrate blood brain barrier penetration

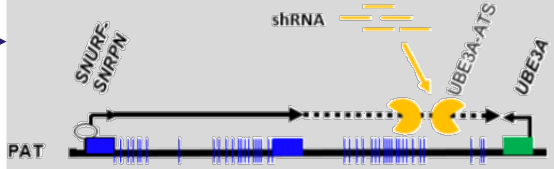
"Trial Ready" Community Toolbox

KIF1A
KIF1A.ORG



Natural history and pathology mapping for rare CNS disorders

Replicable approach for interdicting similar genes/pathways



Cassette style approach to targets and shRNA

Partner targets with non-like modalities

Discover, translate & accelerate into human trials

©2022 OVID THERAPEUTICS INC. | ALL RIGHTS RESERVED

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

©2022 OVID THERAPEUTICS INC. | ALL RIGHTS RESERVED

Ovid™ Therapeutics

Thank you.

MAY 2022