NEWS RELEASE

Ovid Therapeutics Presents Pre-Clinical Study Results Demonstrating OV329 Does Not Accumulate in Animal Eyes in Contrast with Vigabatrin

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- Study found OV329 cleared and remained undetectable in the retina, eye, and brain tissues of mice, unlike vigabatrin which has repeatedly shown to preferentially accumulate in mouse retinas, eyes, and other tissues
- OV329's potency, mechanism of inhibition, short half-life, rapid tissue elimination and prolonged pharmacodynamic effect suggests it delivers a differentiated ocular safety and efficacy profile from vigabatrin
- A Phase 1 trial evaluating OV329 in healthy volunteers is on-track for completion in late 2024 and will evaluate safety and two biomarkers for target engagement and evidence of clinical effect

NEW YORK, Sept. 26, 2024 (GLOBE NEWSWIRE) -- Ovid Therapeutics Inc. (NASDAQ: OVID), a biopharmaceutical company dedicated to improving the lives of people affected by rare epilepsies and brain conditions presented the results of a head-to-head animal study evaluating whether OV329 could be found to accumulate in mouse retinas and brains, as has been previously shown to occur with vigabatrin (VGB) the only FDA-approved GABA-aminotransferase (GABA-AT) inhibitor.

The findings, which were presented via a poster at the Epilepsy Pipeline Conference, found that OV329 cleared and remained undetectable in the retinas, eyes, and brains of mice after 48 hours of continuous exposure via a sub-cutaneous osmotic pump, suggesting a lack of accumulation. In contrast, ocular accumulation of VGB was confirmed within this period. Full results from the head-to-head animal study will be presented at the 2024 American Epilepsy Society conference in December.

These results replicate previously published findings that indicate VGB preferentially and rapidly accumulates

within mouse tissue and plasma, including retina, visual cortex, and brain at subtherapeutic doses (70 mg/kg).1,2 In contrast, a therapeutic dose of OV329 in animals (5 mg/kg) did not show signs of ocular accumulation in the same study design. These results complement previously presented studies which showed that therapeutic doses of OV329 (3 mg/kg) did not result in retinal tissue pathology at 45 days in Sprague Dawley rats, an animal model that investigates structural and functional ocular toxicity.3 In contrast, VGB did show retinal cell degradation at the therapeutic dose in animals of 300 mg/kg at 45 days.

“Today’s findings suggest a compelling and potentially differentiated profile for OV329. A combination of attributes potentially enables OV329 to deliver an anti-convulsant effect at lower, safer, and non-sedative doses without the same ocular changes seen with vigabatrin,” stated Zhong Zhong, Ph.D. and Chief Scientific Officer of Ovid Therapeutics. “Specifically, OV329’s potency, tissue-clearance, mechanism of inhibition, pharmacokinetic and pharmacodynamic profile suggest it is highly efficient at binding to, and inhibiting the GABA-AT enzyme, and then, rapidly clearing the tissue. We believe this unique combination of drug characteristics may have application in a variety of conditions characterized by hyperexcitation,” he added.

STUDY METHODS AND RESULTS

At the Epilepsy Pipeline Conference, Ovid presented results from a preclinical head-to-head study intended to evaluate the tissue distribution of OV329 and VGB following continuous infusion via a subcutaneous osmotic pump in mice for two days. This study replicates and builds upon published research examining how VGB preferentially accumulates in the retina, eye, and visual cortex.1,2 The presented study tested OV329 at 5 mg/kg/day, compared to 80 mg/kg/day of VGB. Notably, the dose studied for OV329 led to exposures above those expected to be reached in humans, while VGB was tested at the established therapeutic exposure level in humans.

- OV329 was not observed to accumulate in the retina, eye, or brain. The concentrations of OV329 in target tissues were below the lower limit of quantification, or undetectable, indicating that OV329 clears and does not accumulate in the retina, eye, or brain. It is thought that OV329’s short-half-life of 1.5 hours, quick tissue elimination properties, and prolonged pharmacodynamic effect may reduce the risk of ocular accumulation to occur.

- VGB has been shown to accumulate in the eye at sub-therapeutic doses in animals and was associated with ocular toxicity at therapeutic doses in humans. Previous animal studies have demonstrated VGB’s tendency to accumulate preferentially in the retina, eye, visual cortex and brain with significantly higher retina/plasma ratios observed (6.1 ± 0.29).1 VGB also demonstrated a higher preference of the biological active S- (+) enantiomer to accumulate in tissues suggesting the potential for more prominent off target effects.4

OV329 PHASE 1 TRIAL

Ovid anticipates the completion of a Phase 1 single ascending dose (SAD) and multiple ascending dose (MAD) study of OV329 in healthy volunteers in late 2024. This safety and tolerability study is additionally applying magnetic resonance spectrometry and transcranial magnetic stimulation, respectively, as biomarkers of target engagement and potential clinical effect.

The poster presented at the Epilepsy Pipeline Conference can be found under the Posters and Publications section of Ovid's website at **investors.ovidrx.com**

ABOUT OV329

OV329 is a next-generation anti-seizure medicine being developed for the potential treatment of rare and treatment-resistant forms of epilepsy and seizures, such as seizures associated with tuberous sclerosis complex, infantile spasms and conditions with focal onset seizures. OV329 inhibits GABA-AT, which is an enzyme in the brain that catabolizes GABA and thereby increases endogenous levels of GABA, the brain's inhibitory neurotransmitter. By increasing GABA, OV329 is thought to reduce neuronal hyperexcitability and suppress seizures.

OV329 was rationally designed to improve upon and potentially supplant VGB, the only FDA-approved GABA-AT inhibitor. VGB is an approved anti-convulsant for the treatment of infantile spasms and refractory complex partial seizures. Use of VGB has been limited by its Black Box warning for permanent bilateral peripheral visual field constriction, a form of irreversible blindness that occurs in some patients taking the drug. Prior studies have shown OV329 to be 200-to-1,000-fold more potent than VGB. OV329 has been shown to possess favorable tissue clearance characteristics, while delivering prolonged PD effect through both phasic (synaptic) and tonic (extrasynaptically) inhibition, thereby strengthening inhibitory neurotransmission in the neuronal milieu.

About Ovid Therapeutics

Ovid Therapeutics Inc. is a New York-based biopharmaceutical company that is dedicated to improving the lives of people affected by rare epilepsies and brain conditions with seizure symptoms. Ovid is advancing a pipeline of novel, targeted small molecule candidates that modulate the intrinsic and extrinsic factors involved in neuronal hyperexcitability causative of seizures and other neurological symptoms. Ovid is developing: OV888/GV101 capsule, a potent and highly selective rho-associated coiled-coil containing protein kinase 2 (ROCK2) inhibitor, for the potential treatment of cerebral cavernous malformations and other rare central nervous system diseases; OV329, a GABA-AT inhibitor, a potential therapy for treatment-resistant seizures; and OV350, a direct activator of the potassium-chloride co-transporter 2 (KCC2), for the potential treatment of epilepsies and other psychiatric conditions. For more information about these and other Ovid research programs, please visit **www.ovidrx.com**.

Forward Looking Statements

This press release includes certain disclosures by Ovid that contain “forward-looking statements” including, without limitation: statements regarding the potentially differentiated ocular safety and efficacy profile of OV329; the expected timing of completion of Ovid’s Phase 1 SAD and MAD trial evaluating OV329 in healthy volunteers; the therapeutic potential of OV329, including potential anti-convulsant effect, tolerability and non-sedative dosing; the potential application of OV329 to a variety of conditions characterized by hyperexcitation; OV329’s potential as a treatment of rare and treatment-resistant epilepsy and seizures; the potential therapeutic opportunity of OV888/GV101 capsule, OV329 and OV350; and other statements that are not historical fact. You can identify forward-looking statements because they contain words such as “anticipates,” “believes,” “expects,” “intends,” “may,” “plan,” “potentially,” and “will,” and similar expressions (as well as other words or expressions referencing future events, conditions or circumstances). Forward-looking statements are based on Ovid’s current expectations and assumptions. Because forward-looking statements relate to the future, they are subject to inherent uncertainties, risks and changes in circumstances that may differ materially from those contemplated by the forward-looking statements, which are neither statements of historical fact nor guarantees or assurances of future performance. Important factors that could cause actual results to differ materially from those in the forward-looking statements include, without limitation, the risk that results of preclinical studies or earlier clinical trials are not necessarily predictive of future results, our drug candidates may not have favorable results in planned or future preclinical studies or clinical trials, or may not receive regulatory approval. 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 13, 2024, 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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2 Colmers PLW, et al. Sustained Inhibition of GABA-AT by OV329 Enhances Neuronal Inhibition and Prevents Development of Benzodiazepine Refractory Seizures. eNeuro. 2024 Jul
3 Bailer, et al. Progress report on new antiepileptic drugs: A summary of the Sixteenth Eilat Conference on New Antiepileptic Drugs and Devices (EILAT XVI): I. Drugs in preclinical and early clinical development. Epilepsia. 2022 Aug.
4 Walters DC, et al. Preferential accumulation of the active S-(+) isomer in murine retina highlights novel mechanisms of vigabatrin-associated retinal toxicity. Epilepsy Res. 2021 Feb.

Source: Ovid Therapeutics Inc.