



Ovid Therapeutics Presents New Data Demonstrating Potential of TAK-935/OV935 as a Novel Treatment for Developmental and Epileptic Encephalopathies at the American Epilepsy Society (AES) Annual Meeting

- Phase 1 Clinical Trials of TAK-935/OV935 Demonstrated a Strong Safety Profile and Well Characterized Pharmacokinetic Profile, Supporting Further Clinical Advancement -

- Results Support Plasma 24S-hydroxycholesterol (24HC) as a Potential Biomarker of TAK-935/OV935 Treatment -

NEW YORK, Dec. 03, 2017 (GLOBE NEWSWIRE) -- Ovid Therapeutics Inc. (NASDAQ:OVID), a biopharmaceutical company committed to developing medicines for patients with rare neurological diseases, today announced results appearing in five poster presentations, including two Phase 1 clinical trials, two preclinical studies and a dosing model, supporting the clinical advancement of TAK-935/OV935 as a potential treatment for developmental and epileptic encephalopathies. The data were presented at the American Epilepsy Society 71st Annual Meeting, taking place December 1-5, 2017, at the Walter E. Washington Convention Center in Washington, D.C.

In January 2017, Takeda and Ovid Therapeutics formed a global collaboration focused on the clinical development and commercialization of TAK-935/OV935, a potent and highly selective cholesterol 24-hydroxylase (CH24H) inhibitor being investigated in adults with developmental and epileptic encephalopathies. These results are the first TAK-935/OV935 data to be presented by Takeda and Ovid Therapeutics.

“We are pleased with the results of these studies, which validate CH24H inhibition as a novel target for epilepsy treatment and also form a strong foundation supporting our ongoing clinical

development and biomarker strategy for TAK-935/OV935,” said Dr. Emiliangelo Ratti, head of Takeda’s Central Nervous System Therapeutic Area Unit. “Not only do these results reinforce the safety and tolerability of this potential therapy, but they also provide vital information for the design and dosing of future clinical trials.”

TAK-935/OV935 was investigated in healthy subjects in two randomized, double-blind, placebo controlled Phase 1 clinical trials, including a single ascending dose study and a multiple ascending dose study. Results demonstrated that TAK-935/OV935 had a generally favorable safety profile and was well tolerated up to a dose of 1,350 mg in the single ascending dose study and at once daily doses up to 400 mg in the multiple ascending dose study. Additionally, a clinical trial simulation was conducted using the results from four Phase 1 clinical trials to create a population pharmacokinetic (PK) model. Together with the results from preclinical studies that demonstrated a correlation between systemic TAK-935/OV935 exposure and reduction in brain 24HC levels, this model can be used to guide dosing in future trials of TAK-935/OV935.

“These results support our broader development strategy for TAK-935/OV935, which includes development in younger patient populations since developmental and epileptic encephalopathies are often diagnosed early in life. We believe providing an early intervention may alter the course of the disease,” said Amit Rakhit, M.D., MBA, chief medical and portfolio management officer of Ovid Therapeutics. “We are excited about these data and the potential of TAK-935/OV935 to be an impactful treatment for people with developmental and epileptic encephalopathies who currently do not have sufficient therapeutic options. We are looking forward to the results of our ongoing Phase 1b/2a clinical trial of TAK-935/OV935 in adults with developmental and epileptic encephalopathies, which are expected in 2018.”

As part of Takeda and Ovid’s development strategy, plasma 24HC is being assessed as a potential biomarker for TAK-935/OV935. The results of clinical and preclinical studies demonstrate that there is a dose-dependent correlation between TAK-935/OV935 treatment and reduction of plasma 24HC levels. This may support the use of plasma 24HC concentration as a biomarker that can inform the design of future clinical trials and help clinicians individualize the dosing of TAK-935/OV935.

The poster presentations are listed below. The full abstracts can be found at:

https://www.aesnet.org/annual_meeting/

- **Clinical Trial Simulations Using a Pharmacokinetic/Enzyme Occupancy/Pharmacodynamic Model of TAK-935, a Cholesterol 24S-hydroxylase Inhibitor (#344434)**
 - The model-based approach allowed integration of pertinent PK and pharmacodynamic data to select a dose and a regimen that optimize response while ensuring an acceptable safety and tolerability profile in pediatric patients.
- **Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of Single Ascending Doses of TAK-935 in Healthy Subjects (#344521)**
 - In a Phase 1, randomized, double-blind, placebo-controlled study, single ascending oral doses of up to 1,350 mg of TAK-935/OV935 or placebo were administered to 48 healthy subjects under fasted conditions.
 - TAK-935/OV935 was shown to have an acceptable safety profile and was well tolerated

following a single administration up to 1,350 mg.

- **Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of Multiple Ascending Doses of TAK-935 in Healthy Subjects (#344533)**
 - In a Phase 1, randomized, double-blind, placebo-controlled study, 40 healthy subjects received ascending oral doses of TAK-935/OV935 (100, 300, 400 or 600 mg once daily or 300 mg twice daily) for 14 days.
 - TAK-935/OV935 had an acceptable safety profile and was well tolerated following once-daily doses of up to 400 mg for 14 days in healthy subjects. Plasma 24HC concentrations decreased by 47 to 63 percent from baseline in a dose-dependent fashion and achieved steady state levels by day 7.
- **Evaluation of Pharmacodynamic Effects of Cholesterol 24-hydroxylase Inhibitor TAK-935 and Its Target Engagement in Animals (#344659)**
 - Reduction in 24HC levels was highly correlated with TAK-935/OV935 systemic exposures in rodents.
- **Inhibition of Cholesterol 24-hydroxylase is a Novel Pharmacological Strategy for Epilepsy Treatment (#344660)**
 - In the preclinical model, TAK-935/OV935 delayed the onset of seizure development, indicating that an approximate 50 percent reduction in brain 24HC levels can produce a therapeutic benefit.

About Developmental and Epileptic Encephalopathies

The term epileptic encephalopathy includes a group of epilepsy syndromes associated with severe cognitive and behavioral disturbances. The International League Against Epilepsy (ILAE) defines an *epileptic encephalopathy* as a condition in which “the epileptiform EEG abnormalities themselves are believed to contribute to a progressive disturbance in cerebral function.”

These epilepsies cause significant morbidities for patients beyond what might be expected from the known underlying pathology alone and can worsen over time. Developmental and epileptic encephalopathies typically present early in life and are often associated with severe cognitive and developmental impairment in addition to frequent treatment-resistant seizures throughout the person’s lifetime. These disorders vary in age of onset, developmental outcomes, etiologies, neuropsychological deficits, electroencephalographic (EEG) patterns, seizure types and prognosis.

Examples of this category of epilepsy includes the following epilepsy syndromes:

- Early myoclonic encephalopathy (EME)
- Early infantile epileptic encephalopathy (EIEE/Ohtahara syndrome)
- Infantile Spasm (West Syndrome)
- Dravet syndrome (severe myoclonic epilepsy in infancy; SMEI)
- Malignant epilepsy with migrating partial seizures in infancy
- Doose syndrome (myoclonic atstatic epilepsy)
- Myoclonic status in nonprogressive encephalopathies
- Lennox-Gastaut syndrome (LGS)
- Landau-Kleffner syndrome (LKS)
- Epilepsy with continuous spike-waves during slow sleep (CSWS)
- Rasmussen's encephalitis

Despite the availability of medicines for epilepsy, few treatment options are available for epileptic encephalopathies, and novel therapies are needed.

About TAK-935/OV935

TAK-935/OV935, which is being studied in developmental and epileptic encephalopathies, is a potent, highly-selective, first-in-class inhibitor of the enzyme cholesterol 24-hydroxylase (CH24H). CH24H is predominantly expressed in the brain, where it plays a central role in cholesterol homeostasis. CH24H converts cholesterol to 24HC, which then exits the brain into the blood plasma circulation. Glutamate is one of the main neurotransmitters in the brain and has been shown to play a role in the initiation and spread of seizure activity. Recent literature indicates CH24H is involved in over-activation of the glutamatergic pathway through modulation of the NMDA channel, implying its potential role in central nervous system diseases such as epilepsy. To Ovid's knowledge, TAK-935/OV935 is the only molecule with this mechanism of action in clinical development.

TAK-935/OV935 has been tested in preclinical models to provide data to support the advancement of the drug into human clinical studies in patients suffering from rare epilepsy syndromes. A novel proprietary PET ligand, developed by Takeda and Molecular Neuroimaging, LLC (MNI), has been used to determine target occupancy of TAK-935/OV935 in the brain. In addition, the effect of TAK-935/OV935 on CH24H enzyme activity in the brain has been assessed by following measurable reductions in the plasma concentration of 24HC.

TAK-935/OV935 has completed four Phase 1 clinical studies, which have assessed tolerability and target engagement at doses believed to be therapeutically relevant. TAK-935/OV935 is being co-developed by Ovid and Takeda Pharmaceutical Company Limited.

About Ovid Therapeutics

Ovid Therapeutics (NASDAQ:OVID) is a New York-based biopharmaceutical company using its BoldMedicine™ approach to develop therapies that transform the lives of patients with rare neurological disorders. Ovid's drug candidate, OV101, is currently in development for the treatment of Angelman syndrome and Fragile X syndrome. Ovid initiated the Phase 2 STARS trial of OV101 in people with Angelman syndrome in 2017 and completed a Phase 1 trial in adolescents with Angelman syndrome or Fragile X syndrome. Ovid is also developing OV935 in collaboration with Takeda Pharmaceutical Company Limited for the treatment of epileptic encephalopathies and in August 2017 initiated a Phase 1b/2a trial of OV935.

For more information on Ovid, please visit <http://www.ovidrx.com/>.

Forward-Looking Statements

This press release includes certain disclosures that contain "forward-looking statements," including, without limitation, statements regarding progress, timing, scope and results of clinical trials for Ovid's product candidates, the development of therapies for younger patients, the provision of access to effective therapies, and the execution of Ovid goals for not only OV101 but also OV935, and the use of plasma concentration 24HC concentration as a biomarker to inform future clinical trial designs and to help clinicians individualize the dosing of TAK-935/OV935. You can identify forward-looking statements because they contain words such as

“will,” “believes” 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 are set forth in Ovid’s filings with the Securities and Exchange Commission, including its Quarterly Report on Form 10-Q for the quarter ended September 30, 2017, under the caption “Risk Factors.” Ovid assumes no obligation to update any forward-looking statements contained herein to reflect any change in expectations, even as new information becomes available.

Contacts

Investors:

Burns McClellan

Steve Klass, 212-213-0006

Sklass@burnsmc.com

Media:

Pure Communications, Inc.

Katie Engleman, 910-509-3977

katie@purecommunicationsinc.com