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Ovid Therapeutics Presents Additional Data and Analyses from the Phase 2 STARS Clinical Trial with OV101 for the Treatment of Angelman Syndrome at the 65th AACAP Annual Meeting

-- Additional data and analyses suggest that in the OV101 15 mg once-daily dose group, changes in sleep parameters and motor domains contributed to the statistically significant improvement in overall clinical global symptoms (CGI-I) observed in previously announced topline data --

-- Conference call and webcast today at 10:30 a.m. EDT during 65th American Academy of Child and Adolescent Psychiatry Annual Meeting --

SEATTLE, Oct. 25, 2018 (GLOBE NEWSWIRE) -- Ovid Therapeutics Inc. (NASDAQ: OVID), a biopharmaceutical company committed to developing medicines that transform the lives of people with rare neurological diseases, today announced additional exploratory efficacy data and analyses from the company's Phase 2 STARS trial that further support the potential of OV101, a novel selective extrasynaptic GABA_A receptor agonist that is being investigated to treat Angelman syndrome. Angelman syndrome is a life-long genetic disorder that is characterized by a variety of signs and symptoms, and for which there are no FDA-approved medicines or an established treatment paradigm.

The additional efficacy data and analyses are being presented in a poster today at the American Academy of Child and Adolescent Psychiatry (AACAP) annual meeting by Alex Kolevzon, M.D., professor of psychiatry and pediatrics at the Icahn School of Medicine at Mount Sinai. The additional data and analyses revealed changes in certain sleep parameters and motor domains in both adults and adolescents in the OV101 15 mg once-daily dose group as further described in the detailed STARS data summary below. Ovid believes these observed changes may have contributed to the statistically significant improvement observed in the clinician-rated clinical global impressions of improvement (CGI-I) symptoms overall in the 15 mg once-daily OV101 dose group compared to placebo after 12 weeks of

treatment, as reported in the topline data from the STARS trial on August 6, 2018. CGI-I is a global measure commonly used in clinical trials that allows the clinician to capture improvement in a constellation of clinical symptoms.

“Angelman syndrome is an extremely complex disorder in which any given patient may present with a variety of symptoms with different degrees of severity,” said Dr. Kolevzon. “These additional data from the STARS trial are encouraging, particularly the efficacy signals observed across the domains of sleep and motor, which appear to have driven the overall improvements seen in CGI-I. There are no established tools or endpoints to measure a drug’s effect on signs and symptoms of Angelman syndrome, and the information gained from the Phase 2 STARS trial establishes the potential of OV101 to offer a clinically meaningful benefit specific to people living with Angelman syndrome.”

“STARS was informed by extensive collaboration with the Angelman community,” said Jeremy Levin, DPhil, MB, BChir, chairman and chief executive officer of Ovid Therapeutics. “The data presented today contribute to a greater understanding and appreciation of the outcomes observed after administration of OV101 on key clinical aspects of Angelman syndrome. These results, together with those reported in August 2018, will help inform our discussions with the FDA when we meet with them later this year.”

Topline Data Announced August 6, 2018

Primary endpoint: Safety and Tolerability

The study met its primary endpoint of safety and tolerability given that the adverse events (AEs) with OV101 treatment were similar to placebo treatment, with the majority of AEs being mild. OV101 showed a favorable risk profile and was well tolerated through 12 weeks of treatment. The most common AEs reported in the trial were vomiting, somnolence, irritability, aggression, and pyrexia. Serious adverse events (SAEs) of seizure were reported in two patients with a previous history of seizures: one patient in the once-daily (QD) dose experienced a seizure and that was deemed unrelated to study drug; one patient experienced a seizure in the twice-daily (BID) dose group and that was assessed as possibly related to study drug by the investigator.

Exploratory endpoints:

The STARS trial explored the clinical utility of OV101 on changes in CGI-I, behavior, sleep, and gross and fine motor ability. The study randomized 88 patients and analyses were performed on 87 patients (mean age=22.6), which includes all patients who enrolled in the study and received at least one dose of study drug.

Prespecified analysis outcome

Following 12 weeks of treatment, OV101 showed a statistically significant improvement in CGI-I symptoms overall compared to placebo in a responder analysis ($p=0.0206$, combined dose group, Fisher’s Exact Test) and in the 15 mg QD dose group ($p=0.0006$, mixed model repeated measures (MMRM) analysis¹).

Remaining prespecified analyses were conducted across subsets in the domains of behavior [Aberrant Behavior Checklist (ABC-C), Anxiety, Depression and Mood Scale (ADAMS)], sleep (e-diary – caregiver reported sleep changes) and motor [Modified Performance-Oriented Mobility Assessment–Gait tool (mPOMA- G)], and analyses of these endpoints did not show a statistically significant difference from placebo.

¹MMRM (mixed model repeated measures), is a rigorous statistical analysis that accounts for multiplicity; it includes fixed effects for visit, treatment, age (adult vs. adolescent) and visit by treatment interaction.

Comprehensive Data Presented Today at AACAP Results from Additional Exploratory Endpoints and Further Analyses of Domains of Sleep, Motor, Behavior and Quality of Life

Overall, the results indicate that OV101 seems to positively impact several relevant clinical features of Angelman syndrome (global functioning, sleep, motor disruption) and therefore support further clinical development of OV101 in Angelman syndrome.

Sleep Domain

Change from Baseline in Sleep Efficacy at Week 12 (MMRM Analysis)

An actigraphy watch was used to assess sleep parameters including latency to sleep, mean daytime sleepiness and changes in sleep efficiency. Approximately 45 percent (n=39) of patients tolerated the device. The clinician-rated clinical impression of sleep domain was analyzed using MMRM, to assess overall sleep. Sleep as reported by caregiver diary showed no changes.

Latency to Sleep Onset:

- Latency to sleep onset (LSO) is the duration of time it takes a person to transition from full wakefulness to sleep. Sleep dysfunction has been identified as clinically relevant in Angelman syndrome, and the observed reduction in LSO may therefore be indicative of target engagement.
- LSO was improved in OV101 15 mg QD dose group compared with placebo (Diff=-25.7 minutes, p=0.0147).

Mean Daytime Sleepiness and Sleep Efficiency:

- Reduction in mean total sleep time during day (~50 minutes) and increase in sleep efficiency (3.65%) were seen in OV101 15 mg QD dose group compared with placebo.

Overall Sleep:

- An improvement in clinical impression of sleep domain at Week 12 was observed in the OV101 15mg QD group compared to placebo (Diff=-0.77, p=0.0141). The OV101 BID

group did not separate from placebo (Diff= -0.45, p=0.1407).

Gross and Fine Motor Domain

Change from Baseline in Motor Efficacy at Week 12 (MMRM Analysis)

Bayley Scales of Infant and Toddler Development Third Edition (BSID-III) was used to assess changes of ≥ 3 points from baseline (post-hoc, responder analysis).

- Changes in overall motor response (54%, p=0.0889; n=14/26) and gross motor only (36%, p=0.0522; n= 9/25) were observed in OV101 15 mg QD dose group compared to placebo at Week 12. No change was seen in fine motor ability alone with either dose.

PEDI-CAT mobility and daily activity summary score (post-hoc analysis)

- Signals were observed in gross motor scores in OV101 15 mg QD group compared with placebo in: mobility score (0.91+/- 0.281 versus 0.08 +/- 0.294; mean +/- standard error (SE); per protocol set; p=0.0475), and in daily activity score (0.79 +/- 0.340 versus 0.00 +/- 0.300; per protocol set; p=0.0869).

Disability Index of CHAQ:

- A signal (n=24, p=0.0704) was observed in the Disability Index of the Childhood Health Assessment Questionnaire (CHAQ) in the OV101 15 mg QD dose group compared to placebo.

ZenoTM Walkway:

- Reduction in mean cadence (n=24, p=0.0340) and stride velocity (n=24, p=0.0406) was observed in the OV101 15 mg QD dose group compared to placebo.

Behavior Domain

In a post-hoc analysis, among patients who showed changes on the CGI-I, the Parent Global Impression (PGI) scale reported improvements in communication, challenging behavior, and anxiety. However, no significant differences were found on the ABC-C and ADAMS.

Quality of Life Domain

No changes were found between groups on EuroQoL 5-Dimension (EQ-5D-SL), Short-Form Health Survey (SF-36), or PGI.

Phase 2 STARS Trial Design

STARS was a 12-week, double-blind, placebo-controlled Phase 2 study. Eighty-eight patients (adults, n=66; adolescents, n=22) aged 13 to 49 years of age diagnosed with Angelman syndrome. The study randomized patients to one of three arms: once-daily (QD) dose of OV101 at night (15 mg), twice-daily (BID) dose of OV101 (10 mg in the morning and 15 mg at night), and placebo.

The primary endpoint of the trial was to assess the safety and tolerability of OV101 compared to placebo. The STARS trial also explored the clinical utility of OV101 on improvements in clinical global impressions, behavior, sleep, and gross and fine motor skills.

ELARA 1-year Extension Study

In the fourth quarter of 2018, Ovid expects to initiate ELARA, an open-label extension study that will enable individuals with Angelman syndrome who completed any prior OV101 study to be eligible to receive the investigational medicine. The study will use once-daily dosing and will assess long term safety and tolerability in addition to efficacy measures.

Conference Call and Webcast Details

Ovid Therapeutics will host a live conference call and webcast today, October 25, 2018, at 10:30 a.m. EDT. The live webcast can be accessed by visiting the Investors section of the company's website at investors.ovidrx.com. Please connect at least 15 minutes prior to the live webcast to ensure adequate time for any software download that may be needed to access the webcast. Alternatively, please call 866-830-1640 (U.S.) or 210-874-7820 (International) to listen to the live conference call. The conference ID number for the live call is 7685159. A replay of the webcast will be available on the company's website for two weeks following the live conference call.

About Angelman Syndrome

Angelman syndrome is a genetic disorder that is characterized by a variety of signs and symptoms. Characteristic features of this disorder include delayed development, intellectual disability, severe speech impairment, problems with movement and balance, seizures, sleep disorders and anxiety. The most common cause of Angelman syndrome is the loss of function of the gene that codes for ubiquitin protein ligase E3A (UBE3A), which plays a critical role in nerve cell communication, resulting in impaired tonic inhibition. Individuals with Angelman syndrome are highly social with a typical lifespan; however, they require constant support from a network of specialists and caregivers. Angelman syndrome affects approximately 1 in 12,000 to 1 in 20,000 people in the U.S. There are currently no U.S. Food and Drug Administration (FDA)-approved therapies for the treatment of Angelman syndrome.

Angelman syndrome is associated with a reduction in tonic inhibition, a function of the delta (δ)-selective GABA_A receptor that allows a human brain to decipher excitatory and inhibitory neurological signals correctly without being overloaded. If tonic inhibition is reduced, the brain becomes inundated with signals and loses the ability to separate background noise from critical information.

About OV101

OV101 (gaboxadol) is believed to be the only delta (δ)-selective GABA_A receptor agonist in development and the first investigational drug to specifically target the disruption of tonic inhibition, a central physiological process of the brain that is thought to be the underlying cause of certain neurodevelopmental disorders. OV101 has been demonstrated in laboratory studies and animal models to selectively activate the δ -subunit of GABA_A receptors, which are found in the extrasynaptic space (outside of the synapse), and thereby impact neuronal activity through tonic inhibition.

Ovid is developing OV101 for the treatment of Angelman syndrome and Fragile X syndrome to potentially restore tonic inhibition and relieve several of the symptoms of these disorders. In preclinical studies, it was observed that OV101 improved symptoms of Angelman syndrome and Fragile X syndrome. This compound has also previously been tested in over 4,000 patients (over 1,000 patient-years of exposure) and was observed to have favorable safety and bioavailability profiles.

The FDA has granted Orphan Drug and Fast Track designations for OV101 for both the treatment of Angelman syndrome and Fragile X syndrome. The U.S. Patent and Trademark Office has granted Ovid patents directed to methods of treating Angelman syndrome and Fragile X syndrome using OV101. The issued patents expire in 2035.

About Ovid Therapeutics

Ovid Therapeutics (NASDAQ: OVID) is a New York-based biopharmaceutical company using its BoldMedicine™ approach to develop medicines that transform the lives of patients with rare neurological disorders. Ovid has a broad pipeline of potential first-in-class medicines. The company's lead investigational medicine, OV101, is currently in development for the treatment of Angelman syndrome and Fragile X syndrome. Ovid is also developing OV935/TAK-935 in collaboration with Takeda Pharmaceutical Company Limited for the treatment of rare developmental and epileptic encephalopathies (DEE).

For more information on Ovid, please visit <http://www.ovidrx.com/> (https://www.globenewswire.com/Tracker?data=jxvmKyJBmLem-VkVjG91UiR9kZav0S1J5kaBho14yIpAI1-E9EOtZipJLQ802wyCOaz_SM5ZTqxvrBGg1laWkuNKHMHv6E5oWDKMuHt6DwY=).

Forward-Looking Statements

This press release includes certain disclosures that contain “forward-looking statements,” including, without limitation, statements regarding (i) the potential clinical benefit of OV101 to treat patients with Angelman syndrome, (ii) the timing and results of any discussions with regulatory authorities regarding the registrational path for OV101 and approval; and (iii) the timing and scope of any future clinical trials for OV101. 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 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.

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[data=eMt_49Xxld36hiRjiFQbCh9JnRyWHT6gz90A6LWC80JVAwDsE8-owgDScS8nyV1HmNOoh3hPhhkvrsm28pDYgTiZWQLmymDtqCmPvMziQa4=](https://www.globenewswire.com/Tracker?data=eMt_49Xxld36hiRjiFQbCh9JnRyWHT6gz90A6LWC80JVAwDsE8-owgDScS8nyV1HmNOoh3hPhhkvrsm28pDYgTiZWQLmymDtqCmPvMziQa4=))
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