Clearside Biomedical Announces Positive Safety Results from Cohort 1 of OASIS Phase 1/2a Clinical Trial of CLS-AX (axitinib injectable suspension) for the Treatment of Wet AMD

June 15, 2021

- CLS-AX 0.03 mg dose delivered via suprachoroidal injection was well-tolerated with no treatment related adverse events -

- Initiating Cohort 2 patient screening for 0.1 mg dose in June 2021 -

ALPHARETTA, Ga., June 15, 2021 (GLOBE NEWSWIRE) -- Clearside Biomedical, Inc. (NASDAQ:CLSD), a biopharmaceutical company dedicated to developing and delivering treatments that restore and preserve vision for people with serious back of the eye diseases, announced today positive safety results from Cohort 1 of OASIS, its ongoing Phase 1/2a clinical trial of CLS-AX (axitinib injectable suspension) administered by suprachoroidal injection via Clearside's SCS Microinjector ® in six patients (n=6) with neovascular age-related macular degeneration (wet AMD).

The primary endpoints were achieved in Cohort 1, as the initial lowest planned dose of 0.03 mg CLS-AX was well tolerated with no serious adverse events and no drug related treatment emergent adverse events observed throughout the study period. There were no signs of inflammation, no vasculitis, no intraocular pressure (IOP) safety signals, no dispersion of drug into the vitreous, or any other drug related adverse events observed in any of the patients. The OASIS Safety Monitoring Committee has reviewed the data and the trial will advance to Cohort 2. Clearside expects to begin Cohort 2 patient screening for a dose of 0.1 mg CLS-AX in June 2021 with completion of this four month study period expected by the end of the year.

"We are very encouraged by the Cohort 1 results of the OASIS trial and we are immediately beginning Cohort 2 enrollment as planned," said Thomas A. Ciulla, M.D., MBA, Chief Medical Officer and Chief Development Officer. "The initial data from Cohort 1 clearly achieved our safety and tolerability endpoints. While still early and recognizing there are a limited number of patients, we believe the Cohort 1 data supports our hypothesis that the combination of targeted and compartmentalized suprachoroidal delivery and the potent pan-VEGF attributes of axitinib may facilitate an effective treatment option for patients suffering from wet AMD."

The average age of the patients in Cohort 1 was 82 years and all were anti-VEGF treatment-experienced, having undergone numerous injections of standard-of-care anti-VEGF treatments prior to entering the OASIS trial. The mean number of prior anti-VEGF treatments within the twelve months and up to the 3 years prior to the start of the trial was 9.0 injections and 22.5 injections, respectively. All enrolled patients underwent diagnostic imaging at screening, followed by masked reading center confirmation of persistent active disease. The mean central subfield thickness (CST) of the macula was 231 µm (range 208 - 294 µm). The mean baseline best corrected visual acuity (BCVA) score as measured by Early Treatment Diabetic Retinopathy Study (ETDRS) letters, at the start of the trial was 59.0 (range 29 - 74).

As part of the trial design, at the initial visit, the six treatment-experienced patients in Cohort 1 received a standard-of-care, single intravitreal injection of 2 mg aflibercept. One month later, the mean ETDRS BCVA score for all patients remained stable, changing only by -0.2 letters, and patients then received a single suprachoroidal dose of 0.03 mg CLS-AX. One month after receiving CLS-AX, five of six patients exhibited improvement in BCVA, each gaining four or more letters, with mean ETDRS BCVA score of all patients increasing by +4.7 letters (p=0.029, post hoc, unadjusted). In Cohort 1: no patients required additional treatment with aflibercept at the one-month visit post CLS-AX; two patients went three months post CLS-AX without additional treatment with aflibercept and BCVA improved by 5 and 7 ETDRS letters for these patients; and four patients received additional treatment with aflibercept at the two month visit post CLS-AX. The mean CST was stable within 50 µm for all Cohort 1 patients both at one month post 2 mg aflibercept and at one month post 0.03 mg CLS-AX.

"CLS-AX was well-tolerated and these initial results in this heavily treatment-experienced group of wet AMD patients are promising. I look forward to the continued clinical advancement of CLS-AX at the planned higher doses to further explore potential benefits in visual acuity, ocular anatomy and durability," added Mark R. Barakat, M.D., Director of Research, Retinal Consultants of Arizona; Clinical Assistant Professor, University of Arizona College of Medicine, Phoenix.

The current OASIS trial protocol includes a CLS-AX dose of 0.1 mg for Cohort 2 and 0.3 mg for Cohort 3, which equates to 3.3x and 10.0x the Cohort 1 dose of 0.03 mg. The Company expects to add a three-month extension study to follow patients in Cohort 2 and Cohort 3. Combined data from the multiple cohorts of the OASIS trial is planned to be presented at future medical meetings.

Information on Clearside's pipeline, including the CLS-AX program and Cohort 1 top-line results, are included in the Company's corporate presentation which may be accessed on the Clearside website under the Investors section: Events and Presentations.

About the OASIS Phase 1/2a Clinical Trial

OASIS is an open-label, single dose-escalation Phase 1/2a trial in wet AMD patients to assess the safety and tolerability of three increasing doses of CLS-AX administered by suprachoroidal injection via Clearside's SCS Microinjector ®. Eligible patients are those who demonstrate stable visual acuity following two or more previous injections with an intravitreal anti-VEGF agent. All enrolled patients undergo diagnostic imaging on screening, followed by masked reading center confirmation of persistent active disease.

Enrolled patients initially receive aflibercept at the first visit followed by a single dose of CLS-AX at the second visit one month later. The primary endpoint for the trial will assess the safety and tolerability of CLS-AX for the three months following the administration of CLS-AX, and secondary endpoints will evaluate the pharmacokinetics, visual function, ocular anatomy, and the need for additional treatment with intravitreal aflibercept during the three-month period.

The study design is planned with 3 cohorts of approximately 5 patients each (n=15). Cohort 1 participants received the lowest dose, 0.03 mg of axitinib

delivered via suprachoroidal injection, and the trial is proceeding to Cohort 2 with a dose of 0.1 mg of axitinib. Dose escalation to the next Cohort follows review of the safety data by the Safety Monitoring Committee and their recommendation to advance to the next higher dose cohort. Additional information on the Phase 1/2a trial can be found on https://clinicaltrials.gov (NCT04626128).

About CLS-AX (axitinib injectable suspension)

Axitinib is a tyrosine kinase inhibitor (TKI) currently approved to treat renal cell cancer that achieves pan-VEGF blockade, directly inhibiting VEGF receptors-1, -2, and -3 with high potency and specificity. Clearside believes this broad VEGF blockade may have efficacy advantages over existing retinal therapies by acting at a different level of the angiogenesis cascade and may benefit patients who sub-optimally respond to current, more narrowly focused anti-VEGF therapies. Preclinical studies by independent investigators have shown pharmacodynamic effects with reduced growth of experimental neovascularization and decreased fluorescein leakage.

CLS-AX (axitinib injectable suspension) is a proprietary suspension of axitinib for suprachoroidal injection. With suprachoroidal administration of axitinib, there is targeted delivery of this pan-VEGF inhibitor to affected tissue layers for potential efficacy benefits, as well as prolonged chorioretinal tissue levels for potential durability benefits. Suprachoroidal injection of this proprietary suspension of axitinib has demonstrated meaningful potential in preclinical studies in multiple species.

About Clearside's Suprachoroidal Space (SCS ®) Injection Platform and SCS Microinjector®

Clearside's patented, proprietary suprachoroidal space (SCS ®) injection treatment approach offers unprecedented access to the back of the eye where sight-threatening disease often occurs. The company's unique platform is inherently flexible and intended to work with established and new formulations of medications. Clearside's proprietary SCS Microinjector ® can be used to inject a wide variety of drug candidates that are specifically formulated to be delivered via suprachoroidal injection. The SCS Microinjector provides targeted delivery to potentially improve efficacy and compartmentalization of medication to reduce or eliminate toxic effects on non-diseased cells. The SCS Microinjector is composed of a syringe and two 30-gauge hollow microneedles of varying lengths, each less than 1.2 millimeters, within a custom-designed hub that optimizes insertion and suprachoroidal administration of drugs.

About Clearside Biomedical

Clearside Biomedical, Inc. is a biopharmaceutical company dedicated to developing and delivering treatments that restore and preserve vision for people with serious back of the eye diseases. Clearside's proprietary SCS Microinjector ® targets the suprachoroidal space (SCS®) and offers unique access to the macula, retina and choroid where sight-threatening disease often occurs. The Company's SCS injection platform is an inherently flexible, in-office, non-surgical procedure, intended to provide targeted delivery to the site of disease and to work with both established and new formulations of medications. For more information, please visit www.clearsidebio.com.

Cautionary Note Regarding Forward-Looking Statements

Any statements contained in this press release that do not describe historical facts may constitute forward-looking statements as that term is defined in the Private Securities Litigation Reform Act of 1995. These statements may be identified by words such as "believe", "expect", "may", "plan", "potential", "will", and similar expressions, and are based on Clearside's current beliefs and expectations. These forward-looking statements include statements regarding the clinical development, including the timing of initiation of Cohort 2 patient screening for the OASIS clinical trial, and the potential benefits of CLS-AX and therapies using Clearside's SCS Microinjector ®. These statements involve risks and uncertainties that could cause actual results to differ materially from those reflected in such statements. Risks and uncertainties that may cause actual results to differ materially include uncertainties inherent in the conduct of clinical trials, Clearside's reliance on third parties over which it may not always have full control, uncertainties regarding the COVID-19 pandemic and other risks and uncertainties that are described in Clearside's Annual Report on Form 10-K for the year ended December 31, 2020, filed with the U.S. Securities and Exchange Commission (SEC) on March 15, 2021, and Clearside's other Periodic Reports filed with the SEC. Any forward-looking statements speak only as of the date of this press release and are based on information available to Clearside as of the date of this release, and Clearside assumes no obligation to, and does not intend to, update any forward-looking statements, whether as a result of new information, future events or otherwise.

Source: Clearside Biomedical, Inc.

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