Clearside Biomedical Announces Positive 6-Month Results from OASIS Extension Study with Suprachoroidal CLS-AX (axitinib injectable suspension) in Wet AMD

February 2, 2023

- Suprachoroidal CLS-AX Resulted in Favorable Safety Data, Durability and Biologic Effect Over 6 Months in Treatment-Experienced Anti-VEGF Sub-Responders -

- 67% of Extension Study Participants Went at Least 6 Months Without Needing Additional Treatment -

- Extension Participants Experienced a 77 - 85% Reduction in Treatment Burden Over 6 Months -

- Webcast and Conference Call Today at 8:30 A.M. ET Hosted by Management and Including Key Opinion Leader, Mark R. Barakat, M.D. -

ALPHARETTA, Ga., Feb. 02, 2023 (GLOBE NEWSWIRE) -- Clearside Biomedical, Inc. (Nasdaq: CLSD), a biopharmaceutical company revolutionizing the delivery of therapies to the back of the eye through the suprachoroidal space (SCS®), announced today positive results from the Extension Study of its OASIS Phase 1/2a clinical trial of CLS-AX (axitinib injectable suspension) administered by suprachoroidal injection via Clearside's SCS Microinjector ® in neovascular age-related macular degeneration (wet AMD) participants. These results include the final six-month data from all participants in the Extension Study and augment the previously reported 3-month results and interim extension data.

Thomas A. Ciulla, M.D., M.B.A., Chief Medical Officer and Chief Development Officer, said, "The positive data from our OASIS Extension Study reinforces our belief that CLS-AX has the potential to reduce treatment burden in patients with wet AMD while maintaining stable visual acuity. In all participants in the trial, CLS-AX was well tolerated and demonstrated an excellent safety profile across all timepoints and doses. Importantly, the full extension data reported today showed promising durability with 67% of participants going at least six months without additional treatment, and 50% of participants going beyond six months. With these favorable data, we are actively preparing for and expect to initiate a randomized, controlled, double-masked, Phase 2b clinical trial, called ODYSSEY, in the first quarter of this year, with the primary endpoint readout anticipated in mid-2024."

George Lasezkay, Pharm.D., J.D., Clearside's President and Chief Executive Officer, commented, "We made tremendous progress in 2022 with the commercialization of our first suprachoroidal product by Bausch + Lomb and the positive safety and durability results from our Phase 1/2a OASIS trial. As we advance our CLS-AX wet AMD program with the initiation of our ODYSSEY Phase 2b trial, we continue to build on this significant momentum and will further increase awareness of the broad potential in delivering therapies to the back of the eye using our proprietary SCS® platform technology."

"This CLS-AX data demonstrating stable visual acuity with durability up to and beyond six months is very encouraging as we look to lower the treatment burden for wet AMD patients. As the management of wet AMD expands to include therapeutic options with different mechanisms of action, such as axitinib and faricimab, it makes sense to compare outcomes to these therapies in future clinical trials. CLS-AX, with suprachoroidal delivery and an alternate mechanism of action from standard of care anti-VEGF products, may prove to be a differentiated therapy for wet AMD and other retinal diseases," added Mark R. Barakat, M.D., Director of Retinal Research Institute, Retinal Consultants of Arizona, and Clinical Assistant Professor of Ophthalmology, University of Arizona College of Medicine - Phoenix.

Conference Call & Webcast Details

Clearside will host a webcast and conference call with accompanying slides today at 8:30 a.m. ET, including comments by management and retinal expert, Dr. Mark R. Barakat. The live and archived webcast may be accessed on the Clearside website under the Investors section: Events and Presentations. The live call can be accessed by dialing (888) 506-0062 (domestic) or (973) 528-0011 (international) and entering conference code: 676850.

OASIS Data Summary

The OASIS Phase 1/2a trial is complete for both the 3-month dose-escalation portion and the 3-month Extension Study. The study included four cohorts at the following doses: Cohort 1 at 0.03 mg; Cohort 2 at 0.1 mg; Cohort 3 at 0.5 mg; Cohort 4 at 1.0 mg. Participants from Cohorts 2, 3 and 4 who rolled over into the Extension Study were followed for a total of 6 months after a single dose of CLS-AX. Participants enrolled in OASIS were heavily anti-VEGF treatment experienced with active disease[1] at screening, which was confirmed by an independent reading center.

Safety and Tolerability Results in All Cohorts in the 3-Month Study (n=27) & 6-Month Extension Study (n=14)

- No serious adverse events (SAEs), no treatment emergent adverse events (TEAEs) related to study treatment, and no dose limiting toxicities.
- No adverse events related to inflammation, vasculitis or vascular occlusion.
- No vitreous "floaters" or dispersion of CLS-AX into the vitreous.
- No retinal detachments, endophthalmitis, or adverse events related to intraocular pressure.

Durability in the 6-Month Extension Study in Cohorts 3 & 4 at higher doses (n=12)

- 77% - 85% reduction in treatment burden was observed compared to the average monthly injections in the six months

before CLS-AX administration.

- Participants not requiring additional therapy:
  - ≥ 3 Months: 11/12 (92%)
  - ≥ 4 Months: 10/12 (83%)
  - ≥ 6 Months: 8/12 (67%)
  - > 6 Months: 6/12 (50%)

Biologic Effect in the 6-Month Extension Study in Cohorts 3 & 4 (n=12)

- CLS-AX showed signs of biologic effect with stable mean best corrected visual acuity (BCVA) and stable mean central subfield thickness (CST) to the 6-month timepoint.
- On Optical Coherence Tomography (OCT) images, anatomical signs of TKI biologic effect were observed in anti-VEGF treatment experienced sub-responders.

About the Planned ODYSSEY Phase 2b Clinical Trial

ODYSSEY will be a multi-center, randomized, double-masked Phase 2b clinical trial to assess a total of approximately 110 treatment-naïve participants with wet AMD. In addition to loading doses of faricimab, participants will be randomized 1:1 to receive either CLS-AX administered by suprachoroidal injection via Clearside's SCS Microinjector ®, or intravitreal faricimab dosed per approved prescribing information[2]. The objectives of the trial are to demonstrate comparable mean change in BCVA from baseline between treatment arms with improved durability and reduced treatment burden for the CLS-AX arm, measured at 6 and 12 months.

Trial Design

- Loading Doses: Participants in both arms will receive 4 monthly faricimab (6.0 mg) loading doses. In the CLS-AX arm, participants will also receive one dose of CLS-AX (1.0 mg) at the same visit as the third loading dose of faricimab (baseline).
- Monthly Disease Activity Assessments (DAA): DAAs begin 2 months after the last faricimab loading dose to determine need for retreatment. The retreatment criteria include decrease in BCVA, increase in CST, or new macular hemorrhage[3].
- Subsequent Treatments:
  - In the CLS-AX arm, participants are required to be dosed with CLS-AX at least every 6 months following the last CLS-AX dose. Participants may be dosed sooner than 6 months with CLS-AX if retreatment criteria is met during a DAA.
  - In the faricimab arm, participants are required to be dosed with faricimab at least every 4 months (per label). Participants may be dosed sooner with faricimab if retreatment criteria is met during a DAA. If participants are retreated earlier than 4 months, they will continue to receive further doses of faricimab at that dosing interval for the remainder of the study (per label).
- Key inclusion criteria: Treatment naïve wet AMD participants with subfoveal choroidal neovascularization (CNV) secondary to wet AMD, and BCVA of 78–24 letters.
- Endpoints: Primary endpoint is the mean change from baseline in BCVA at 6 months (Week 24 Visit) from baseline. Key secondary endpoints include mean change in CST and treatment burden reduction as measured by total injections. All endpoints will be measured at 6 months (Week 24 Visit) and 12 months (Week 48 & 52 Visits combined) from baseline.

As of December 31, 2022, Clearside's cash and cash equivalents totaled $48.3 million. This amount is an unaudited and preliminary estimate that (i) represents the most current information available to management as of the date hereof, (ii) is subject to completion of financial closing and auditing procedures that could result in significant changes to the estimated amount, and (iii) does not present all information necessary for an understanding of Clearside's financial condition as of, and results of operations for the year ended, December 31, 2022. Accordingly, you should not place undue reliance on this preliminary estimate.

About the OASIS Phase 1/2a Clinical Trial

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

The study included four cohorts totaling 27 patients at the following doses: Cohort 1 at 0.03 mg; Cohort 2 at 0.1 mg; Cohort 3 at 0.5 mg; Cohort 4 at 1.0 mg. Enrolled patients received 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 was assessment of the safety and tolerability of CLS-AX for the 3 months following the administration of CLS-AX, and secondary endpoints evaluated the pharmacokinetics, visual function, ocular anatomy, and the need for additional treatment with intravitreal aflibercept.

A 3-month Extension Study was conducted to follow patients in Cohorts 2, 3 and 4 who chose to continue for a total of six months. Additional information on the Phase 1/2a trial can be found on clinicaltrials.gov NCT04626128 and the extension study can be found at NCT05131646.

About CLS-AX (axitinib injectable suspension)

CLS-AX (axitinib injectable suspension) is a proprietary suspension of axitinib for suprachoroidal injection. 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. Suprachoroidal injection of this proprietary suspension of axitinib has demonstrated meaningful potential in preclinical studies in multiple species and in a Phase 1/2a clinical trial. With suprachoroidal administration of axitinib, there is the potential to achieve prolonged duration and targeted delivery to affected tissue layers. Clearside is developing CLS-AX as a long-acting therapy for the treatment of retinal diseases.

About Neovascular Age-Related Macular Degeneration (wet AMD)

Age-related macular degeneration causes a progressive loss of central vision and is the most common cause of legal blindness in individuals over age 55. Wet AMD is generally caused by abnormal blood vessels that leak fluid or blood into the macula, the part of the retina responsible for central vision, and accounts for the majority of vision loss in patients with this disorder. In the U.S., approximately 11 million patients are living with AMD, and about 20% have the wet form. Current treatments require life-long, frequent injections to maintain efficacy. This treatment regimen tends to cause a treatment burden for patients resulting in reduced compliance and under-treatment leading to potentially limited outcomes.

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, Inc.

Clearside Biomedical, Inc. is a biopharmaceutical company revolutionizing the delivery of therapies to the back of the eye through the suprachoroidal space (SCS®). Clearside's SCS injection platform, utilizing the Company's proprietary SCS Microinjector ®, enables an in-office, repeatable, non-surgical procedure for the targeted and compartmentalized delivery of a wide variety of therapies to the macula, retina or choroid to potentially preserve and improve vision in patients with sight-threatening eye diseases. Clearside is developing its own pipeline of small molecule product candidates for administration via its SCS Microinjector and strategically partners its SCS injection platform with companies utilizing other ophthalmic therapeutic innovations. Clearside's first product, XIPERE® (triamcinolone acetonide injectable suspension) for suprachoroidal use, is commercially available in the U.S. For more information, please visit www.clearsidebio.com.

[1] Active persistent disease defined as active subfoveal choroidal neovascularization (CNV) secondary to AMD in the study eye confirmed by an independent reading center as leakage from a subfoveal CNV on fluorescein angiography and intra-retinal or sub-retinal fluid on OCT central subfield.
[2] Refer to Prescribing Information for VABYSMO® (faricimab-svoa) injection, for intravitreal use. VABYSMO is a registered trademark of Genentech.

[3] Retreatment criteria include:

- Increase ≥75 µm in CST compared with the lowest CST value recorded at either of the previous 2 scheduled visits, or
- Increase >50 µm in CST compared with the average CST value over the previous 2 scheduled visits, or
- Decrease ≥5 letters in BCVA compared with the average BCVA value over the previous 2 scheduled visits, owing to nAMD disease activity (as determined by the Investigator), or
- Decrease ≥10 letters in BCVA compared with the highest BCVA value recorded at either of the previous 2 scheduled visits, owing to nAMD disease activity (as determined by the Investigator), or
- Presence of new macular hemorrhage (as determined by the Investigator), owing to nAMD disease activity.

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 of CLS-AX, timeline for initiating the ODYSSEY Phase 2b clinical trial for CLS-AX, the expected timing of data from the ODYSSEY clinical trial, Clearside's cash and cash equivalents as of December 31, 2022 and the potential benefits of CLS-AX and other product candidates 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, 2021, filed with the U.S. Securities and Exchange Commission (SEC) on March 11, 2022, Clearside's Quarterly Report on Form 10-Q for the quarter ended September 30, 2022 filed with the SEC on November 9, 2022 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.

Investor and Media Contacts:

Jenny Kobin
Remy Bernarda
ir@clearsidebio.com

(678) 430-8206

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