Clearside Biomedical Announces Positive Results in Safety, Durability and Biologic Effect in OASIS Phase 1/2a Clinical Trial of Suprachoroidal CLS-AX (axitinib injectable suspension) in Wet AMD Patients

November 9, 2022

- Primary Safety Endpoint Achieved at all Timepoints with All Doses Well-Tolerated and No Treatment Related or Serious Adverse Events -

- Cohorts 3 and 4 Demonstrated Promising Signs of Durability, Biologic Effect, and a Meaningful Reduction in Treatment Burden -

- Final 6-Month Data from Extension Study Expected in Q1 2023 -

- Expect to Initiate Phase 2 Clinical Trial in Q1 2023 -

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

OASIS Demographics and Wet AMD History

Wet AMD Disease Characteristics	COHORT 1: 0.03 mg	COHORT 2: 0.1 mg	COHORT 3: 0.5 mg	COHORT 4: 1.0 mg	All Cohorts
No. of participants	6	5	8	8	27
Mean age (range), years	81.8 (66-93)	78.2 (65-90)	86.3 (75-97)	76.5 (66-83)	80.9 (65-97)
Mean baseline best corrected visual acuity (range), letters	59.0 (29-74)	65.6 (52-75)	58.5 (37-74)	65.8 (50-74)	62.1 (29-75)
Mean baseline central subfield retinal thickness (range), µm	231.2 (208-294)	209.4 (184-227)	202.0 (175-238)	218.8 (152-295)	214.8 (152-295)
Mean duration of wAMD diagnosis (range), months	50.13 (12.4-110.3)	49.78 (24.7-81.3)	66.64 (6.8-102.1)	48.21 (4.5-132.8)	54.39 (4.5-132.8)
Number of anti-VEGF injections reported prior to CLS-AX administration on Day 1, mean (range)	26.8 (7-41)	24.2 (12-39)	37.0 (6-90)	28.8 (5-89)	29.9 (5-90)
Annualized number of anti-VEGF injections prior to CLS-AX administration on Day 1, mean (range)	9.36 (6.3-12.7)	9.54 (5.4-12.2)	8.47 (4.9-11.8)	11.96 (8.9-13.6)	9.90 (4.9-13.6)

OASIS Demographics and Wet AMD History

ALPHARETTA, Ga., Nov. 09, 2022 (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 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) patients. Trial results include final 3-month data from all 4 cohorts, and interim data from the Extension Study that follows participating patients for a total of 6 months after a single dose of CLS-AX.

Thomas A. Ciulla, MD, MBA, Chief Medical Officer and Chief Development Officer, commented, "We are strongly encouraged by the results we reported today which highlight the potential use of CLS-AX, a highly potent tyrosine kinase inhibitor combined with targeted SCS delivery, in serious retinal disease. In the four dose-escalating cohorts of the OASIS trial, we enrolled a total of 27 highly treatment-experienced wet AMD patients with active disease at screening. CLS-AX was well tolerated and demonstrated a positive safety profile across all timepoints and doses. Interim data from the Extension Study in Cohorts 3 and 4 showed the supplemental anti-VEGF injection-free rate up to each visit was 88% (7 of 8 patients) to Month 5 and 75% (3 of 4 patients) to Month 6, and at least a 90% reduction in treatment burden to date compared to the patients' 6-month anti-VEGF therapy prior to receiving CLS-AX. In addition, there were observable signs of biologic effect with stable mean Best Corrected Visual Acuity (BCVA) and stable mean Central Subfield Thickness (CST) throughout OASIS and the Extension Study at all timepoints to date."

"The positive safety results seen in all four cohorts, combined with evidence that CLS-AX showed biologic effect in a difficult to treat patient population, supports our belief that CLS-AX has the potential to treat retinal diseases with a repeatable, reliable, and validated in-office delivery approach using our SCS Microinjector. We are finalizing the optimal path forward for CLS-AX in retinal diseases including wet AMD and/or diabetic retinopathy. We are actively preparing for and expect to initiate a randomized, controlled Phase 2 clinical trial in the first quarter of 2023," Dr. Ciulla concluded.

"Real world outcomes in patients with wet AMD continue to be poor due to high treatment burden and missed visits, which drives retinal specialists to look for better treatment options that are safe, effective, and provide a better quality of life for our patients. This CLS-AX data is quite promising as the optical coherence tomography (OCT) images show a biologic effect while extending the time for retreatment out for several months. CLS-AX, combined with the convenience and reliability of the suprachoroidal injection procedure, may be a valid future approach for treating a variety of retinal disorders," added Arshad M. Khanani, MD, MA, FASRS, Managing Partner, Director of Clinical Research, and Director of Fellowship at Sierra Eye Associates, and Clinical Associate Professor at the University of Nevada, Reno School of Medicine.

Summary of OASIS Data

The OASIS 3-month open-label, dose-escalation Phase 1/2a trial is complete. There is an ongoing additional 3-month Extension Study, for a total of 6 months of follow-up after a single dose of CLS-AX in patients from Cohorts 2, 3 and 4. All patients enrolled in OASIS were heavily anti-VEGF treatment experienced with active disease[1] at screening, which was confirmed by an independent reading center. Patient demographics and wet AMD treatment history are summarized in the following chart:

Wet AMD Disease Characteristics	COHORT 1: 0.03 mg	COHORT 2: 0.1 mg	COHORT 3: 0.5 mg	COHORT 4: 1.0 mg	All Cohorts
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Safety and Tolerability Results (in All Four Cohorts, n=27)

- CLS-AX met the trial's primary endpoint, demonstrating a positive safety profile at all doses and timepoints.
- There were no serious adverse events, no treatment emergent adverse events, no dose limiting toxicities, no adverse events related to inflammation, vasculitis or vascular occlusion.
- There were no vitreous "floaters" or dispersion of CLS-AX into the vitreous, no retinal detachments or endophthalmitis, and no adverse events related to intraocular pressure.

Durability (in Cohorts 3 & 4)

In OASIS to the 3-month timepoint (n=16):

- 69% of patients did not receive additional therapy
- 92% of patients did not receive additional therapy per protocol criteria
- 73% reduction in treatment burden from the average monthly injections in the three months before CLS-AX administration

In the ongoing Extension Study, based on interim data as of 10/27/22 (n=12):

- Supplemental anti-VEGF injection-free rate up to each visit
  - To Month 5: 88% (7/8) of patients did not receive additional therapy
  - To Month 6: 75% (3/4) of patients did not receive additional therapy
- 90% reduction in treatment burden from the average monthly injections in the six months before CLS-AX administration
- 8 patients remain in the Extension Study with final 6-month data expected in Q1 2023

Biologic Effect (in Cohorts 3 & 4)

- In OASIS, CLS-AX showed signs of biologic effect with stable mean BCVA and stable mean CST to the 3-month timepoint.
- In the ongoing Extension Study, CLS-AX showed signs of biologic effect with stable mean BCVA and stable mean CST to the 6-month timepoint (based on interim data as of 10/27/22).
- On OCT, anatomical signs of TKI biologic effect were observed in anti-VEGF treatment experienced sub-responders.

[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).

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. Arshad Khanani. 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: 111701.

OASIS Phase 1/2a Clinical Trial Design

OASIS is an open-label, dose-escalation Phase 1/2a trial in wet AMD patients to assess the safety and tolerability of a single dose of CLS-AX administered by suprachoroidal injection via Clearside's SCS Microinjector ®. Eligible patients were those who demonstrated stable visual acuity following two or more previous injections with an intravitreal anti-VEGF agent. All enrolled patients 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 to follow patients in Cohorts 2, 3 and 4 is ongoing. 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

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.

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, timeline for initiating the Phase 2 clinical trial for and the potential benefits of CLS-AX and 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 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.

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A photo accompanying this announcement is available at https://www.globenewswire.com/NewsRoom/AttachmentNg/81c6d49e-47c5-4a15-b1af-877abe0ba001