Clearside Biomedical Presents Compelling Data at The Association for Research in Vision and Ophthalmology (ARVO) 2023 Annual Meeting

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- Suprachoroidal delivery of small molecule suspensions demonstrated targeted, compartmentalized and durable drug delivery -

ALPHARETTA, Ga., April 27, 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 that several key poster presentations were delivered on the Company's suprachoroidal injection delivery platform at The Association for Research in Vision and Ophthalmology (ARVO) 2023 Annual Meeting.

"Our presentations at ARVO continue to demonstrate that Clearside is leading the way in suprachoroidal delivery of agents to the back of the eye," said, George Lasezkay, Pharm.D., J.D., President and Chief Executive Officer. "In the studies presented, SCS delivery of small molecule suspensions offered targeted, compartmentalized, and durable drug delivery to the chorioretina. In addition, our commercial partner presented data on the adoption of XIPERE® (triamcinolone acetonide injectable suspension) for suprachoroidal use, which continues to garner broad acceptance by the retinal community."

"The promising data from our Phase 1/2a OASIS trial in wet AMD showed that CLS-AX had an excellent safety profile and that Extension Study participants maintained their visual acuity while experiencing a meaningful reduction in treatment burden. We are now looking to expand upon these results in ODYSSEY, our randomized, double-masked, Phase 2b clinical trial that we expect to initiate this quarter," concluded Dr. Lasezkay.

Title: Safety and Tolerability Study of Suprachoroidal Injection of CLS-AX in Neovascular AMD Patients with Persistent Activity Following Anti-VEGF Therapy (OASIS, NCT04626128; Extension Study NCT05131646)

Presented by lead author: Dennis M. Marcus, M.D. Southeast Retina Center

Summary: Dr. Marcus presented the results of OASIS, Clearside's Phase 1/2a clinical trial in neovascular age related macular degeneration (wet AMD) with CLS-AX (axitinib injectable suspension). Participants in the study had persistent, active disease and were heavily treatment experienced anti-VEGF sub-responders. CLS-AX administered via suprachoroidal (SCS) injection for was safe and well-tolerated in all cohorts.

The Extension Study in cohorts 3 and 4, exhibited early signs of durability and reduction in treatment burden with participants experiencing a 77% - 85% reduction in treatment burden. Importantly, a post hoc analysis of CLS-AX also showed a biologic effect at higher doses with stable best corrected visual acuity and central subfield thickness.

Title: Suprachoroidal delivery of CLS-301, a potent small molecule integrin antagonist, offers multimonth durability and high bioavailability in the chorioretina

Presented by lead author**:** Viral Kansara, Ph.D., Vice President, Preclinical Development, Clearside Biomedical

Summary: The purpose of the study was to assess safety, durability and compartmentalization of a suprachoroidally administered small molecule suspension of a potent integrin antagonist (CLS-301) in a preclinical model. Integrins play a major role in diverse biologic as well as pathologic processes such as cell adhesion/migration, angiogenesis, and immune responsiveness. The suspension was delivered using Clearside's SCS Microinjector®, an office-based procedure for SCS delivery. In the study, SCS delivery of an integrin inhibitor was well tolerated and offered targeted, compartmentalized, and durable drug delivery to the chorioretina. This trend is consistent with other small molecule suspensions injected into the SCS. Further preclinical and clinical studies exploring long-term safety, pharmacology and toxicology of integrin inhibitors are warranted.

Title: Early Adoption of Triamcinolone Acetonide Suprachoroidal Injection for Uveitic Macular Edema: A Physician Survey

Presented by lead author**:** Peter Yuwei Chang, M.D., Massachusetts Eye Research and Surgery Institution

Summary: The poster described retina/uveitis specialists who had completed at least 10 suprachoroidal injections of XIPERE and participated in virtual meetings in which they responded to 37 survey questions probing their experience. The findings from the survey of early adopters of XIPERE suggest suprachoroidal injection was easy to learn and patient improvements in vision and macular edema aligned with findings in clinical registration trials.

Clearside's medical meeting presentations can be accessed on the Company's Publications and Presentations page.

About CLS-AX (axitinib injectable suspension)

CLS-AX (axitinib injectable suspension) is an investigational proprietary suspension of axitinib for suprachoroidal injection. Axitinib is a tyrosine kinase inhibitor (TKI), currently approved as an oral tablet formulation to treat advanced renal cell carcinoma, 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 wet AMD clinical trial, in which CLS-AX was well tolerated and demonstrated an excellent safety profile. With suprachoroidal administration of axitinib, Clearside believes 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 the OASIS Phase 1/2a Clinical Trial

OASIS was an open-label, single 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.

OASIS was a 3-month trial, followed by a 3-month Extension Study. The trial 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 at screening, which was confirmed by an independent reading center.

Safety and Tolerability Results in All Cohorts in OASIS (n=27) and 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 the 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 BCVA and stable mean 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 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 deliver a wide variety of drug candidates into the suprachoroidal space, providing targeted delivery to potentially improve efficacy and compartmentalization of medication to reduce or eliminate toxic effects on non-diseased cells. The SCS Microinjector system is composed of a syringe, a custom-designed hub and two 30-gauge hollow microneedles of varying lengths, each less than 1.2 millimeters, optimizing insertion and suprachoroidal administration of drugs.

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 XIPERE® (triamcinolone acetonide injectable suspension) for suprachoroidal use

XIPERE® (triamcinolone acetonide injectable suspension) for suprachoroidal use, formerly known as CLS-TA, is a proprietary suspension of the corticosteroid triamcinolone acetonide for administration to the suprachoroidal space for the treatment of macular edema associated with uveitis. Bausch + Lomb, a leading global eye health company dedicated to helping people see better to live better, has the exclusive license for the commercialization and development of XIPERE in the United States and Canada. Arctic Vision, a specialty ophthalmology company based in China, has the exclusive license for the commercialization and development of XIPERE, which they refer to as Arcatus™, in Greater China, South Korea, Australia, New Zealand, India and the ASEAN Countries. XIPERE was approved by the U.S. Food and Drug Administration in October 2021 and is commercially available in the U.S.

Important Safety Information about XIPERE®

Indication
XIPERE® (triamcinolone acetonide injectable suspension) for suprachoroidal use is a corticosteroid indicated for the treatment of macular edema associated with uveitis.

IMPORTANT SAFETY INFORMATION
Patients should be monitored following injection for elevated intraocular pressure. See Dosage and Administration instructions in full Prescribing Information.

- XIPERE is contraindicated in patients with **active or suspected ocular or periocular infections** including most viral diseases of the cornea and conjunctiva, including active epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, varicella, mycobacterial infections, and fungal diseases.
- XIPERE is contraindicated in patients with known **hypersensitivity to triamcinolone acetonide** or any other components of this product.
- Use of corticosteroids may produce cataracts, increased intraocular pressure, and glaucoma. Use of corticosteroids may enhance the establishment of secondary ocular infections due to bacteria, fungi, or viruses, and should be used cautiously in patients with a history of ocular herpes simplex.
- Hypothalamic-pituitary-adrenal (HPA) axis suppression, Cushing's syndrome, and hyperglycemia can occur following administration of a corticosteroid. Monitor patients for these conditions with chronic use.
- In controlled studies, the most common ocular adverse reactions were increased ocular pressure, non-acute (14%), eye pain, non-acute (12%), cataract (7%); increased intraocular pressure, acute (6%), vitreous detachment (5%), injection site pain (4%) conjunctival hemorrhage (4%), visual acuity reduced (4%), dry eye (3%), eye pain, acute (3%), photophobia (3%), and vitreous floaters (3%), and in 2% of patients: uveitis, conjunctival hyperaemia, punctate keratitis, conjunctival oedema, meibomianitis, anterior capsule contraction, chalazion, eye irritation, eye pruritus, eyelid ptosis, photopsia, and vision blurred.

  The most common non-ocular adverse event was headache (5%).
- Corticosteroids should be used during pregnancy or nursing only if the potential benefit justifies the potential risk to the fetus or nursing infant.

To report SUSPECTED ADVERSE REACTIONS, contact Bausch + Lomb at 1-800-321-4576 or FDA at 1-800-FDA-1088 or visit www.fda.gov/medwatch.

Please click here for full Prescribing Information.

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. The Company's lead program, CLS-AX (axitinib injectable suspension), for the treatment of neovascular age-related macular degeneration (wet AMD), is in Phase 2 clinical testing. Clearside developed and gained approval for its first product, XIPERE® (triamcinolone acetonide injectable suspension) for suprachoroidal use, which is available in the U.S. through a commercial partner. Clearside also strategically partners its SCS injection platform with companies utilizing other ophthalmic therapeutic innovations. For more information, please visit www.clearsidebio.com.

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, and the potential benefits, of CLS-AX and therapies using Clearside's SCS Microinjector ® as well as the timeline for initiating the ODYSSEY Phase 2b clinical trial for CLS-AX. 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 and other risks and uncertainties that are described in Clearside's Annual Report on Form 10-K for the year ended December 31, 2022, filed with the U.S. Securities and Exchange Commission (SEC) on March 14, 2023 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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