Clearside Biomedical Delivers Podium and Poster Presentations at the American Society of Retina Specialists (ASRS) Annual Meeting

October 13, 2021

Multiple clinical data presentations demonstrate the potential of the suprachoroidal injection platform as a flexible, in-office, non-surgical procedure across multiple chorioretinal diseases

ALPHARETTA, Ga., Oct. 13, 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 that multiple presentations were given at the American Society of Retina Specialists (ASRS) Annual Meeting and at the OIS Retina Summit at ASRS, which took place October 7 - 12, 2021 in San Antonio, TX.

“The data presented at both ASRS and last week’s Retina Society meetings continue to demonstrate that our proprietary in-office suprachoroidal space (SCS®) injection treatment approach offers unprecedented targeted access to the back of the eye to treat a variety of serious retinal diseases,” said Thomas A. Ciulla, M.D., MBA, Chief Medical Officer and Chief Development Officer. “Together with our partners, positive data has been presented utilizing our SCS Microinjector® to deliver small molecules, gene therapy, and virus-like drug conjugates in multiple diseases, including uveitic macular edema, wet-AMD, diabetic retinopathy, and choroidal melanoma. We remain encouraged by these promising results as we continue to advance our own suprachoroidal clinical development programs and broaden our reach in other indications.”

Dr. Ciulla continued, “At ASRS, REGENXBIO presented positive initial data from their ongoing Phase II ALTITUDE™ trial of RGX-314 for the treatment of diabetic retinopathy using our SCS Microinjector® for in-office suprachoroidal delivery of their gene therapy. RGX-314 was well tolerated in 15 patients in Cohort 1 with no drug-related serious adverse events and no intraocular inflammation observed. It was also encouraging to see that there was a treatment effect after only three months. In addition, our partner Aura Biosciences presented their first data set on suprachoroidal delivery of AU-011, their novel virus-like drug conjugate for the treatment of primary choroidal melanoma, the most common intraocular tumor in adults. In their Phase 2 trial, there have been no treatment-related serious adverse events, dose limiting toxicities, or grade 3 adverse events observed thus far. This favorable safety profile to date may improve the therapeutic index, optimize treatment parameters and potentially lead to improved visual outcomes compared to intravitreal administration. These promising results presented by our partners further support our belief in the usefulness of our suprachoroidal injection platform and the SCS Microinjector with a wide variety of drug candidates.”

Preceding the ASRS meeting, Dr. Ciulla presented a corporate overview during the OIS Retina Summit highlighting the potential of suprachoroidal delivery, as well CLS-AX (axitinib injectable suspension), a proprietary suspension of axitinib, a potent pan-VEGF inhibitor, which is currently being evaluated in a Phase 1/2a clinical trial, entitled OASIS, for the treatment of age-related macular degeneration (wet AMD).

ASRS presentations were as follows:

Title: Suprachoroidal Administration of Small Molecule Suspensions:
Pre-Clinical Results Correlate to Clinical Trial Outcomes
Lead Author: James C Major, Jr., MD, PhD, FASRS
Conclusions: Multiple small molecule suspensions were evaluated in this study, including the corticosteroid triamcinolone acetonide, the tyrosine kinase inhibitor (TKI) axitinib, a complement inhibitor, and a plasma kallikrein inhibitor. Suprachoroidal delivery of these agents was investigated based on their potential for targeted delivery to affected tissues for efficacy, compartmentalization away from unaffected tissues for safety, and durability to address treatment burden. Optical coherence tomography (OCT) images demonstrated a definitive expansion of the suprachoroidal space both anteriorly and posteriorly to the optic nerve head just minutes after suprachoroidal injection. Suprachoroidal injection of small molecule concentrations were similar in both the retina and RPE/Choroid/sclera tissues. Favorable results from preclinical studies of a triamcinolone acetonide suspension (CLS-TA) translated to favorable clinical trial results for macular edema associated with non-infectious uveitis. There is potential for similar read-through of preclinical studies in the four current clinical trials enrolling patients utilizing suprachoroidal injection with the SCS Microinjector®: CLS-AX (axitinib injectable suspension) for wet AMD; viral vector RGX-314 for wet AMD and diabetic retinopathy; and viral-like drug conjugate AU-011 for choroidal melanoma.

Title: Safety of the Suprachoroidal Injection Procedure Via Microinjector across Three Retinal Disorders
Lead Author: Allen Hu, MD
Conclusions: In this analysis, safety data from the day of the procedure was compiled from 621 patients (1,274 suprachoroidal injections) in eight clinical trials utilizing CLS-TA. The suprachoroidal injections were performed across three disease states: noninfectious uveitis, diabetic macular edema, and retinal vein occlusion. There were no serious adverse events (SAEs) involving lens injury, suprachoroidal hemorrhage, endophthalmitis, or retinal tears in any patient receiving one or more suprachoroidal injections. Three SAEs of interest in both the study and control arms were all deemed “not treatment related” by a masked investigator. Overall, the safety profile of the suprachoroidal injection procedure with a microinjector is not clinically meaningfully different than the intravitreal injection as reported in registration trials involving intravitreal anti-VEGF injections alone.

Title: Comparison of Suprachoroidal and Intravitreal Injection Flow Mechanics Analyzed via Multimodal Imaging
Lead Author: Shree Kurup, MD, FACP
Conclusions: This presentation compared suprachoroidal and intravitreal injections using several multimodal imaging diagnostics to demonstrate the injection flow differences between the two procedures. During an intravitreal injection, a bolus of dye was seen in the porcine vitreous cavity. In contrast, during a suprachoroidal injection, spreading of the dye was observed circumferentially and posteriorly towards the back of the eye, between the sclera and choroid. In the study, an endoscope was also placed within the vitreous cavity to film, in real time, both intravitreal and suprachoroidal

injections. Suprachoroidal injection showed localized tissue depression, then expansion with no needle penetration through the choroid and retina. Imaging of suprachoroidal injections demonstrate acute opening of the suprachoroidal space, circumferential, posterior spread of injectate, and compartmentalization of injectate to posterior tissues. In summary, these multimodal imaging methodologies support the potential of suprachoroidal injections to target affected tissue layers in chorioretinal disorders.

Title: OCT Anatomic & Temporal Biomarkers in Uveitic Macular Edema
Lead Author: Dilraj S. Grewal, MD
Conclusions: In clinical practice, physicians often base treatment decisions on best corrected visual acuity (BCVA) and/or OCT assessment. There is limited information on longitudinal structure-function correlations in uveitic macular edema (UME). This study assessed these relationships, focusing on baseline anatomic features with potential prognostic value for visual response. This post hoc analysis of 198 eyes evaluated two Phase 3, 24 week UME clinical trials with CLS-TA (PEACHTREE and AZALEA). The study evaluated clinically relevant and prognostic relationships between BCVA and OCT-assessed features of macular edema including ellipsoid zone integrity, the presence and location of cystoid spaces, and the presence and location of subretinal fluid. Importantly, this analysis showed that eyes with early anatomic response demonstrated better BCVA response at 24 weeks, and that anatomic response may precede visual response in UME by one month or more among patients treated with CLS-TA. A manuscript describing these results has received favorable review in the *American Journal of Ophthalmology*, a prestigious peer-reviewed Medline-indexed journal.

Title: Post Hoc Analysis of Suprachoroidal CLS-TA versus Real World Rescue Therapies for Uveitic Macular Edema: Safety and Visual Function
Lead Author: Steven Yeh, M.D.
Conclusions: In this post hoc analysis of the PEACHTREE trial, visual function and safety outcomes of unrescued CLS-TA subjects were compared to rescued subjects in the control group. Unrescued CLS-TA subjects experienced statistically significant greater reduction in central subfield thickness and trended towards greater improvement in BCVA compared with control subjects rescued with therapies reflecting current clinical treatment. Suprachoroidally administered CLS-TA also appeared to be associated with a lower incidence of intraocular pressure-related safety findings. This post hoc analysis provides a comparison of CLS-TA to a “real world” mix of rescue treatments and corroborates the pre-specified endpoints of the Phase 3 PEACHTREE study. A manuscript describing these results is in press at *Clinical and Experimental Ophthalmology*, a peer-reviewed Medline-indexed journal.

Additional details on Clearside’s presentations can be accessed on the Company’s website here.

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 XIPERE™ (triamcinolone acetonide suprachoroidal injectable suspension)

XIPERE™ (triamcinolone acetonide suprachoroidal injectable suspension), formerly known as CLS-TA, is a proprietary suspension of the corticosteroid triamcinolone acetonide formulated for administration to the suprachoroidal space for the treatment of macular edema associated with uveitis. Clearside’s patented technology is designed to deliver drug to the suprachoroidal space located between the choroid and the outer protective layer of the eye, known as the sclera. Suprachoroidal injection enables the rapid dispersion of medicine to the back of the eye, offering the potential for the medicine to act longer and minimize harm to the surrounding healthy parts of the eye. Bausch + Lomb, a leading global eye health business of Bausch Health Companies Inc. (NYSE/TSX: BHC), 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 in Greater China, South Korea, Australia, New Zealand, India and the ASEAN Countries. XIPERE is not yet approved in any jurisdiction.

About Uveitis and Macular Edema

Uveitis is a set of ocular inflammatory conditions and is one of the leading causes of vision loss, affecting approximately 350,000 patients in the United States and more than one million worldwide. Approximately one-third of these patients develop uveitic macular edema, a build-up of fluid in the macula, the area of the retina responsible for sharp, straight-ahead vision. Macular edema is the leading cause of vision loss and blindness in uveitis patients and can occur from uveitis affecting any anatomic location - anterior, intermediate, posterior or pan. The uveitis market is expected to grow by 2024 to nearly $550 million in the United States and over $1 billion globally.

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. Preclinical results from Clearside and independent investigators have shown pharmacodynamic effects with reduced growth of experimental neovascularization and decreased fluorescein leakage. 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 wet AMD. CLS-AX is currently being investigated in an ongoing US-based, multi-center, open-label, dose-escalation, Phase 1/2a, safety and tolerability study, entitled OASIS, in wet AMD patients, and additional information can be found on https://clinicaltrials.gov (NCT04626128).

About the OASIS Phase 1/2a Clinical Trial

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 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 2 participants received a dose of 0.1 mg of axitinib delivered via suprachoroidal injection. Dose escalation will proceed following review of the Cohort 2 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 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 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 and the potential benefits of XIPERE (formerly known as CLS-TA), CLS-AX and other therapies using Clearside's SCS Microinjector ®, as well as the potential to read-through results of preclinical studies of CLS-TA to the four current clinical trials enrolling patients utilizing suprachoroidal injection with the 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.

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