Clearside Biomedical Features FDA-Approved XIPERE™ in Multiple Presentations at the American Academy of Ophthalmology 2021 and American Uveitis Society Meetings

November 16, 2021

Investigational therapeutics injected via the SCS Microinjector® demonstrate positive clinical data in wet AMD, diabetic retinopathy, and choroidal melanoma in partner programs

ALPHARETTA, Ga., Nov. 16, 2021 (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 multiple presentations were given at the American Academy of Ophthalmology (AAO) 2021, which took place November 12 - 15, 2021 in New Orleans, LA.

“Our presentations at AAO and AUS, combined with the positive data presented by our partners and our ongoing interactions with the leaders in the retinal community, continue to demonstrate the benefits of suprachoroidal administration and the potential for physicians to adopt this procedure in their practices,” said Thomas A. Ciulla, M.D., MBA, Chief Medical Officer and Chief Development Officer. “With the recent FDA approval of XIPERE ™, we now have the first product approved for injection into the suprachoroidal space, and the first therapy approved for patients suffering from macular edema associated with uveitis. As a retinal physician, I am thrilled that my physician colleagues and their patients now have a new, innovative treatment option for those suffering from this serious, potentially blinding disease.”

Dr. Ciulla continued, “Importantly, our partners presented compelling data on the benefits of suprachoroidal delivery of their gene therapy and virus-like drug conjugate product candidates utilizing our SCS Microinjector®. REGENXBIO presented positive initial data from Cohort 2 of AAVIATE® demonstrating that RGX-314 gene therapy was observed to be well tolerated with stable visual acuity and retinal thickness as well as a meaningful reduction in anti-VEGF treatment burden at six months in patients with wet AMD. In addition, further data from Cohort 1 in the Phase 2 ALTITUDE™ trial for the treatment of diabetic retinopathy demonstrated stable visual acuity at three months after one-time treatment of RGX-314. And, Aura Biosciences presented safety results on AU-011, a virus-like drug conjugate for the treatment of choroidal melanoma, reporting that in the initial dose escalation cohorts preliminary results indicate a positive safety and tolerability profile for AU-011 delivered via suprachoroidal administration.”

Clearside AAO Presentations:

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 optical coherence tomography (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 is in press at the *American Journal of Ophthalmology*, a peer-reviewed Medline-indexed journal.

Title: Post-Hoc Analysis of Suprachoroidal CLS-TA vs. Rescue Therapies in Macular Edema associated with Noninfectious Uveitis
Lead Author: Christopher Henry, MD, FASRS
Conclusions: In this post hoc analysis of the PEACTHREE trial, visual function and safety outcomes of unrescued CLS-TA subjects were compared to rescued subjects in the control group reflecting current clinical treatment. Unrescued CLS-TA subjects experienced statistically significant greater mean reduction in central subfield thickness versus controls. Unrescued CLS-TA subjects also trended towards greater mean improvement in BCVA with approximately 52% of those subjects gaining ≥ 15 letters BCVA at 24 weeks versus 37% of subjects in the rescued control group. 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.

Title: Uveitic Macular Edema: Visual Function and Ocular Anatomy by Severity of Vision Loss
Lead Author: Ashvini Reddy, MD
Conclusions: This poster represented a post hoc analysis of the Phase 3 PEACHTREE and AZALEA clinical trial patients who received triamcinolone acetonide injectable suspension for suprachoroidal use (SCS-TA). There were BCVA and anatomic benefits observed in patients who received SCS-TA at 24 weeks regardless of baseline BCVA status. A ceiling effect was observed in BCVA showing that patients with worse BCVA at baseline gained more letters over the 24 weeks than those with better BCVA at baseline. A floor effect was observed in retinal thickness demonstrating that the magnitude of change from baseline decreased as the retina approached normal thickness. Patients with worse BCVA at baseline experienced a greater reduction in CST.

Clearside American Uveitis Society Presentations:

In conjunction with the AAO meeting, Clearside participated in the American Uveitis Society Fall Meeting on Sunday, November 14, 2021.

Title: Suprachoroidal SCS-TA Safety and Efficacy in Macular Edema Associated with Uveitis: Post Hoc Analysis of Clinically Relevant Subgroups
Lead Author: Steven Yeh, MD
Conclusions: These post hoc analyses results corroborate the prospectively planned analyses for PEACHTREE. When unrescued SCS-TA patients are compared to rescued control patients, the analysis showed a significantly greater reduction in CST, a trend towards greater BCVA improvement, and a lower incidence of intraocular pressure elevation and cataract. The post hoc analysis represents a "real world" mix of rescue treatments, with limitations in terms of sample size and variable rescue treatment. The benefit of SCS-TA was noted regardless of administration of systemic corticosteroid or steroid-sparing therapy at baseline versus the control patients.

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 a fluid wave within the suprachoroidal space, underlying the retina. Imaging of suprachoroidal injections demonstrated 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.

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. 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. 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 injectable suspension) for suprachoroidal use

XIPERE™ (triamcinolone acetonide injectable suspension), 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 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 was approved by the U.S. Food and Drug Administration in October 2021.

About PEACHTREE

PEACHTREE, a randomized, masked, sham-controlled Phase 3 trial, enrolled 160 patients with macular edema associated with non-infectious uveitis, and compared XIPERE dosed every 12 weeks to sham control. The PEACHTREE trial met its primary endpoint, with 47% of patients in the XIPERE arm gaining at least 15 letters in best corrected visual acuity from baseline at week 24, compared to 16% of patients in the sham control arm ($p<0.001$), using standardized Early Treatment of Diabetic Retinopathy Study (ETDRS) visual acuity testing. All key secondary and additional endpoints of the PEACHTREE trial were also achieved.

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.

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%), cataract (7%), 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.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

Please click here for full Prescribing Information.

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, was approved by the U.S. Food and Drug Administration in October 2021. 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 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, 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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Source: Clearside Biomedical, Inc.