Clearside Biomedical Pipeline Highlighted in Oral Presentations at the Annual Angiogenesis and Macula Society Meetings

February 25, 2020

– Preclinical data presented on lead development asset, CLS-AX (axitinib injectable suspension) –

– Suprachoroidal injection platform featured in multiple indications including wet AMD, uveitis, diabetic macular edema, and ocular gene therapy –

ALPHARETTA, Ga., Feb. 25, 2020 (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 oral presentations on Clearside's pipeline and proprietary SCS Microinjector™ targeting the suprachoroidal space were given this month at the 17th Annual Angiogenesis Meeting and 43rd Annual Macula Society Meeting.

"February was an extremely productive month for Clearside as our pipeline continues to gain exposure within the physician community, resulting in multiple oral presentations on our programs," said Thomas A. Ciulla, M.D., MBA, Chief Medical Officer. "Importantly, preclinical data was discussed on axitinib for suprachoroidal injection (CLS-AX) supporting the potential for long-acting pan-VEGF inhibition in wet AMD. This positive data provides the rationale to advance this asset that could ultimately lead to improved, long-term, real-world visual outcomes and reduced treatment burden for patients. We expect to submit an Investigational New Drug (IND) application for CLS-AX in mid-2020 and we look forward to initiating Phase 1/2 clinical trial."

Dr. Ciulla concluded, "Numerous presentations were also given on our clinical trials results for XIPERE™ and on the broad applicability of our suprachoroidal injection platform. Also featured was a discussion on the potential advantages of suprachoroidal injection of gene therapy. We believe that suprachoroidal injection can be an in-office procedure, with potential safety benefits for patients by avoiding the risks of sub-retinal administration. We are grateful to the numerous retinal specialists who dedicated their time at these medical meetings and support our efforts to potentially offer improved treatment options for their patients."

CLS-AX (axitinib injectable suspension) & Suprachoroidal Injection

Title:	***Suprachoroidal CLS-AX (axitinib injectable suspension), as a Potential Long-Acting Therapy for Neovascular Age-Related Macular Degeneration (nAMD)***
Author:	Shree K. Kurup, M.D., FACP, Director, Division of Vitreoretinal Diseases, Surgery and Ocular Immunology and Uveitis, University Hospitals
Summary:	Dr. Kurup presented the first public data for Clearside's lead investigational agent, CLS-AX (axitinib injectable suspension) for suprachoroidal injection. Suprachoroidal axitinib has the potential to address primary needs for neovascular AMD patients, as its durability may reduce treatment burden while maintaining vision. Its pan-VEGF inhibition in wet AMD has the potential to be more efficacious than current focused VEGF inhibition approaches. Information from Dr. Kurup's literature review showed there is strong preclinical evidence on the potential efficacy of axitinib as a tyrosine kinase inhibitor (TKI). Specifically: (1) Anti-VEGF A upregulated VEGF-C and VEGF-D, (2) axitinib inhibited neovascularization in the cornea, retina, and choroid, and (3) axitinib had improved biocompatibility with ocular cells relative other TKIs. Suprachoroidal CLS-AX was tested in multiple animal models demonstrating high drug concentration in the retina and choroid-RPE/sclera and lower concentration in the vitreous, and reduction of fluorescein leakage and vessel growth versus control. Across all animal models, suprachoroidal CLS-AX was well tolerated with no signs of toxicity at the intended clinical dose, with sparing of the anterior chamber of the eye and systemic circulation. Overall, suprachoroidal CLS-AX could lead to reduced treatment burden on patients and improved, longer term visual outcomes.

Title:	***Update on Therapeutic Suprachoroidal Injection***
Author:	Thomas A. Albini, M.D., Bascom Palmer Eye Institute; Professor of Clinical Ophthalmology, University of Miami Miller School of Medicine
Summary:	Dr. Albini's presentation reviewed the benefits and broad uses of suprachoroidal injection as it relates to Clearside's pipeline. His discussion focused on the key aspects and uses of this delivery mechanism: 1) small molecule suspension suprachoroidal delivery has shown durability and has been demonstrated with triamcinolone, a tyrosine kinase inhibitor (TKI), and a complement inhibitor; 2) suprachoroidal compartmentalization has potential for safety as demonstrated in the clinical trials with triamcinolone; and 3) the unique ocular distribution of suprachoroidal delivery creates a potential path forward for other therapies including office-based gene therapy and choroidal diseases such as melanoma. Data from Clearside's clinical trials and information on the Company's recent partnerships were also referenced.

XIPERE™ (triamcinolone acetonide suprachoroidal injectable suspension) for Uveitis

Title:	***Front-line Local Therapies for Uveitis: From Clinical Trials to Practice***
Author:	Steven Yeh, M.D., Associate Professor, Emory Eye Center
Summary:	In his presentation, Dr. Yeh discussed the complications of uveitis and current treatment options. He showed multiple Phase 3 studies that have demonstrated the benefits of local corticosteroids administered via novel drug delivery platforms for macular edema due to noninfectious uveitis. Data from Clearside's PEACHTREE and MAGNOLIA clinical trials were highlighted as evidence of the potential effectiveness of suprachoroidal delivery. He also reviewed other agents in development and concluded that the field currently has a

promising outlook for local delivery options for noninfectious uveitis.

Title:	***Intraocular Pressure Following Administration of Suprachoroidal Triamcinolone Acetonide Suspension (CLS-TA): Results from the Phase 3 PEACHTREE Clinical Trial for Uveitis***
Author:	Michael A. Singer, M.D., Medical Center Ophthalmology Associates; Clinical Professor, Ophthalmology, University of Texas Health Science Center
Summary:	Dr. Singer presented preclinical and clinical data which demonstrated that injection into the suprachoroidal space allows for targeted and compartmentalized delivery. Preclinical data showed that posterior tissues, including the sclera/choroid and outer retina contained higher concentration of triamcinolone (TA) when injected suprachoroidally compared to intravitreally. TA was also found in lower concentration in the aqueous humor and iris/ciliary body when delivered suprachoroidally compared to intravitreally. Dr. Singer presented clinical data from the PEACHTREE trial with a focus on intraocular pressure (IOP). With respect to elevated IOP-related adverse events (AEs), the rate was 11.5% in the CLS-TA treatment group (n=11/96) compared to 15.6% in the control group (n=10/64). The number of IOP events in the control group was due to the type of rescue medications delivered, at the discretion of the investigator. Rescue medications were required in 72% (n=46/64) of the patients in the control group and only 13% (n=13/96) in the CLS-TA group. Clinically relevant IOP endpoints were evaluated through week 24. IOP ≥ 30mmHg was observed in only 4.8% of CLS-TA treated eyes (n=4/83) that did not receive rescue medication compared to 10.9% of control eyes (n=5/46) that received rescue. Similarly, IOP lowering medications were used in fewer eyes treated only with CLS-TA (7.2%; n=6/83) compared to the control eyes receiving rescue treatment (13%; n=6/46).

Ocular Gene Therapy

Title:	***Suprachoroidal Delivery for Ocular Gene Therapy: Nonclinical Experiments Evaluating Non-Viral DNA Nanoparticles in Non-Human Primates (NHPs)***
Author:	Mathew W. MacCumber, M.D., Ph.D., Illinois Retina Associates; Professor and Associate Chairman for Research. Department of Ophthalmology, Rush University Medical Center
Summary:	In his presentation, Dr. MacCumber provided the rationale for using suprachoroidal (SC) injection as a potentially safe, targeted and efficient delivery mechanism for gene therapy. He shared information on suprachoroidal delivery of viral vectors in preclinical models, including data from non-human primates showing that suprachoroidal RGX-314 (REGENXBIO) resulted in similar suppression of VEGF-induced vascular leakage as subretinal delivery. He reviewed the potential advantages of DNA Nanoparticles (DNPs), including efficacy in animal models, the ability to transfer large genes, and safety aspects, specifically that DNPs are non-immunogenic and offer the potential for repeat dosing. Dr. MacCumber shared the results of SC injection of Luciferase DNPs in non-human primates, which resulted in luciferase activity observed in the retina and choroid of all eyes that received an SC injection. SC injection of DNPs in non-human primates were generally well tolerated across groups with no significant abnormalities observed.

Diabetic Macular Edema

Title:	***Visual Acuity Outcomes and Anti-Vascular Endothelial Growth Factor Therapy Intensity in Diabetic Macular Edema: A "Real World" Analysis in 28,456 Eyes***
Author:	Thomas A Ciulla, M.D., MBA, Clearside Chief Medical Officer
Summary:	This retrospective analysis was designed to assess visual acuity (VA) outcomes and anti-VEGF treatment intensity in patients with diabetic macular edema (DME). The analysis of 28,456 eyes was performed in treatment-naïve DME patients from 2013 to 2018, using a database of aggregated de-identified electronic medical records. The study found that although the introduction of anti-VEGF agents has led to notably improved outcomes for patients with DME, there are several practical limitations, including the need for frequent injections and incomplete response in some patients. In clinical practice, DME patients undergo fewer anti-VEGF injections and exhibit worse visual outcomes compared to patients in randomized clinical trials. Consequently, "real world" DME treatment compliance can be poor. This analysis demonstrates a large unmet need for DME therapies that address treatment burden and incomplete response.

Title:	***Analysis of OCT Biomarkers in the Randomized Phase 2 TYBEE Trial of Suprachoroidal CLS-TA Plus Aflibercept Compared with Aflibercept Monotherapy for DME***
Lead Author:	Michael S. Ip, M.D., The Doheny Image Reading Center, Doheny Eye Institute, University of California – Los Angeles
Summary:	Dr. Ip and his team evaluated secondary results from Clearside's Phase 2, double-masked, 6-Month TYBEE clinical trial in patients with Diabetic Macular Edema (DME). The trial evaluated combination aflibercept and suprachoroidal CLS-TA treatment compared to aflibercept monotherapy at Week 24. The results from TYBEE demonstrated that fewer treatment visits were needed in the combination arm (2.8) compared to aflibercept monotherapy (4.7), suggesting the potential to address treatment burden. The trial also showed greater reduction of central subfield thickness (CST) with combination treatment (-226.5µm) versus monotherapy (-176.1µm). Analysis of additional anatomical outcomes when comparing the two treatments included disorganization of the retinal inner layers (DRIL) and choroidal vascularity index (CVI). In the trial, changes in DRIL were similar in both arms and DRIL could be a reasonable biomarker to evaluate in future DME clinical trials.

These presentations will be available on Clearside's website in the Publications section under Programs: https://www.clearsidebio.com/publications.htm.

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 by acting at a different level of the angiogenesis cascade, 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 and may benefit patients who sub-optimally respond to current anti-VEGF therapies. Suprachoroidal injection of a proprietary suspension of axitinib has demonstrated meaningful potential in preclinical studies in multiple species. First, axitinib has intrinsic high potency and can achieve pan-VEGF inhibition through receptor blockade. Second, preclinical results from Clearside and outside investigators showed pharmacodynamic effect with reduced growth of experimental neovascularization and decreased fluorescein leakage. Third, suprachoroidal

administration of axitinib can potentially achieve prolonged duration and targeted delivery to affected tissue layers. Clearside is developing CLS-AX as a long-acting therapy for wet AMD and expects to submit an IND application in mid-2020.

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 back of the eye 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 and adequate 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., has the exclusive license for the commercialization and development of XIPERE in the United States and Canada (through a license agreement between Clearside and Bausch Health's affiliate).

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™ targeting the suprachoroidal space (SCS) 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, as well as future therapeutic innovations such as gene therapy. 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 opportunities for expanding Clearside's internal pipeline, the potential benefits of XIPERE and the SCS injection platform, and the development and potential benefits of CLS-AX, including the timing for the IND submission 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, 2018, filed with the U.S. Securities and Exchange Commission ("SEC") on March 15, 2019, Clearside's Quarterly Report on Form 10-Q for the quarter ended September 30, 2019, filed with the SEC on November 6, 2019, 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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