Clearside Biomedical Announces Numerous Presentations at the ARVO 2020 Meeting

June 17, 2020

– Preclinical CLS-AX data demonstrates a potentially long-acting therapy for neovascular age-related macular degeneration –

– Evidence supports the reliability, repeatability, and consistency of Clearside's suprachoroidal injection procedure for chorio-retinal diseases using patented SCS Microinjector® –

ALPHARETTA, Ga., June 17, 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 its proprietary SCS Microinjector ® targeting the suprachoroidal space (SCS®) are available online at the ARVO 2020 Meeting.

Due to COVID-19, the ARVO 2020 Annual Meeting is being held virtually. As a result, abstracts are available online and presentations can be accessed on the ARVOLearn website.

"Clearside's pipeline and our proprietary suprachoroidal delivery system were strongly represented at ARVO this year with thirteen distinct presentations," said Thomas A. Ciulla, M.D., MBA, Chief Medical Officer and Chief Development Officer. "Notably, CLS-AX, our proprietary suspension of axitinib delivered via our SCS Microinjector, demonstrated sustained, well-tolerated and targeted delivery of axitinib to the back of the eye in preclinical studies. In addition, CLS-AX showed inhibition of neovascularization and leakage, as well as durability. With its intrinsic highly potent pan-VEGF inhibition through receptor blockade, CLS-AX has the potential to be an effective therapy for neovascular age-related macular degeneration (nAMD)."

Dr. Ciulla continued, "Another area we are excited to explore, based on data presented at the conference, is complement inhibitors. Preclinical delivery of a complement inhibitor via our SCS Microinjector showed the agent was well tolerated, sustained high drug levels, and merits further studies in the development of long-acting small molecule complement inhibitors for dry AMD. In addition, several presentations featuring delivery of agents via our patented SCS Microinjector continue to support the reliability, repeatability, and consistency of our procedure for the treatment of chorio-retinal diseases. The results continue to demonstrate the robustness of suprachoroidal injection across indications and that the two needle length options successfully accommodate for anatomical variations across patients."

Dr. Ciulla concluded, "We are pleased with the progress of our partner, Aura Biosciences, with whom we have a worldwide licensing agreement for the use of our SCS Microinjector to deliver their proprietary drug candidates into the SCS for the potential treatment of certain ocular cancers, including choroidal melanoma. Aura presented preclinical research at ARVO regarding the ocular distribution and efficacy in a rabbit model of AU-011. According to Aura, the data showed excellent distribution of AU-011 in the SCS and complete necrosis of tumors following laser activation in a rabbit model of choroidal melanoma. Further preclinical studies are currently ongoing, and Aura expects to initiate a Phase 2 clinical study evaluating suprachoroidal delivery of AU-011 during the third quarter of 2020."

CLS-AX (axitinib injectable suspension) and Complement Inhibitors

Title: Suprachoroidal CLS-AX (axitinib injectable suspension), as a Potential Long-Acting Therapy for Neovascular Age-Related Macular Degeneration (nAMD)
Authors: Peter K Kaiser; Thomas Ciulla; Viral Kansara
Conclusions: CLS-AX was well tolerated with durability in the suprachoroidal space. Results from laser choroidal neovascularization studies corroborate other studies, showing inhibition of neovascularization in animal models. Given this pharmacodynamic effect, ability to directly target affected tissues, and intrinsic highly potent pan-VEGF inhibition through receptor blockade, CLS-AX has the potential to be a long-acting therapy for nAMD.
Presentation: https://learning.arvo.org/diweb/catalog/launch/media/eid/5237422
Abstract: https://iovs.arvojournals.org/article.aspx?articleid=2768322&resultClick=1

Title: Pharmacokinetics and Ocular Tolerability of Suprachoroidal CLS-AX (axitinib injectable suspension) in rabbits
Authors: Leroy Muya; Viral Kansara; Thomas Ciulla
Conclusions: Suprachoroidal CLS-AX provided sustained, safe and targeted delivery of axitinib to the back of the eye. Given the durability, intrinsic high potency and pan-VEGF inhibition, suprachoroidal CLS-AX has the potential to be a bi-annual therapy for nAMD.
Presentation: https://learning.arvo.org/diweb/catalog/launch/media/eid/5257731
Abstract: https://iovs.arvojournals.org/article.aspx?articleid=2768760&resultClick=1

Title: Suprachoroidal Delivery of Suspensions of Tyrosine Kinase Inhibitor, Complement Inhibitor, and Corticosteroid: Preclinical and Clinical Correlates
Authors: Debra A Goldstein; Thomas A Ciulla
Conclusions: Suprachoroidal delivery of suspensions of tyrosine kinase inhibitor (TKI), complement inhibitor, and corticosteroid demonstrated prolonged therapeutic levels with the potential for sustained release and high bioavailability, and showed compartmentalization with the potential to minimize adverse effects. These attributes correlate to clinical trial outcomes for corticosteroid; further study of TKI and complement factors suspensions are warranted.
Abstract: https://iovs.arvojournals.org/article.aspx?articleid=2769326&resultClick=1

Title: Ocular Pharmacokinetics and Safety of Suprachoroidal A01017, Small Molecule Complement Inhibitor, Injectable Suspension in

Rabbits
Authors: Shelley E Hancock; Avinash Phadke; Viral Kansara; David Boyer; Jose Rivera; Christopher Marlor; Steven Podos; Jason Wiles; Rick McElheny; Thomas A Ciulla; Mingjun Huang; Mark Cartwright
Conclusions: Suprachoroidal delivery of A01017 suspension, a highly potent complement factor D inhibitor that blocks alternative pathway activity, provided well tolerated, sustained high drug levels in the posterior segment in rabbits, and merits further studies in the development of long-acting small molecule complement inhibitors for dry AMD.
Abstract: https://iovs.arvojournals.org/article.aspx?articleid=2768184&resultClick=1

Treatment Burden and Unmet Need in AMD and Macular Edema

Title: Treatment Burden and Visual Outcomes in Neovascular Age-Related Macular Degeneration (AMD)
Authors: Saira Khanna; Rahul Komati; David Aaron Eichenbaum; Ishani Hariprasad; Thomas A Ciulla; Seenu Hariprasad
Conclusions: Despite the varying durability of the different anti-VEGF agents, there is a positive correlation between the number of injections in 12-months and the change in mean best corrected visual acuity (BCVA) (ETDRS letters). While challenging in practice, frequent treatment regimens have benefits in terms of vision; however, this needs to be mitigated by real-world constraints.
Abstract: https://iovs.arvojournals.org/article.aspx?articleid=2769144&resultClick=1

Title: Visual Acuity Outcomes and Anti-VEGF Intensity in Macular Edema due to RVO: A "Real World" Analysis in 12,214 Eyes
Authors: Thomas A Ciulla
Conclusions: Real-world retinal vein occlusion (RVO) patients with macular edema (ME) experience worse visual outcomes compared with patients in randomized controlled trials. Mean change in visual acuity (VA) correlates with treatment intensity at 1 year. Patients with better VA at presentation tend to be particularly vulnerable to vision loss.
Presentation: https://learning.arvo.org/diweb/catalog/launch/media/eid/5256808
Abstract: https://iovs.arvojournals.org/article.aspx?articleid=2768105&resultClick=1

Gene Therapy

Title: Gene Therapy Biofactory: Mathematical Modeling of Pharmacokinetics
Authors: Lucia Carichino; Giovanna Guidoboni; Viral Kansara; Thomas Ciulla; Alon Harris
Conclusions: The model allowed the estimation of therapeutic protein levels in the retina and vitreous, and showed an aqueous humor level (AHL)-dependent increase of these levels. Future studies are needed to expand the model to account for the retina pigmented epithelium and choroid compartments that contribute to the production of the anti-VEGF protein in this biofactory approach, and whose levels are challenging to extract in the clinical setting. In the future, precision medicine aided by mathematical modeling could be employed after anterior chamber diagnostic testing of pathologic proteins, to select therapeutic options of different gene therapy biofactory approaches.
Presentation: https://learning.arvo.org/diweb/catalog/item?id=5254050
Abstract: https://iovs.arvojournals.org/article.aspx?articleid=2769091&resultClick=1

Suprachoroidal Delivery

Title: Suprachoroidal Delivery with the SCS Microinjector™: Characterization of Operational Forces
Authors: Nathan Fisher; Cherry Wan
Conclusions: Forces to operate the SCS Microinjector using a variety of injectates are far below the international standard recommendations for low-volume hypodermic syringe operation. This may improve the usability of the SCS Microinjector by minimizing resistance forces inherent to the device, therefore allowing the user more accurate tactile feedback with loss of resistance when the suprachoroidal space is reached.
Presentation: https://learning.arvo.org/diweb/catalog/launch/media/eid/5256365
Abstract: https://iovs.arvojournals.org/article.aspx?articleid=2766412&resultClick=1

Title Retrospective Correlation Analysis of Suprachoroidal Injection Experience and Refraction
Authors: Cherry Wan; Barry Kapik; Milan Shah; Christopher R Henry; Charles Clifton Wykoff; Mark Barakat
Conclusions: While these analyses with a 900 µm needle compared to a 1100 µm needle are retrospective with a relatively small sample size, refraction appeared to have little correlation with the needle length used for suprachoroidal injections. This is supported by the literature that scleral thinning with myopia is more prominent along the anterior-posterior axis than around the circumference near the pars plana, where suprachoroidal injections are administered. Taken together, this indicates that suprachoroidal injections with the SCS Microinjector have the potential to reliably and repeatably deliver drugs for chorio-retinal diseases among a wide span of refractive values.
Presentation: https://learning.arvo.org/diweb/catalog/launch/media/eid/5237367
Abstract: https://iovs.arvojournals.org/article.aspx?articleid=2769773&resultClick=1

Title: Post hoc Analysis of Clinical Suprachoroidal Injection Experience Across Indications
Authors: Mark Barakat; Cherry Wan; Barry Kapik
Conclusions: To date, this is the largest aggregate dataset of suprachoroidal clinical injections with mounting evidence pointing to the reliability and consistency of the procedure. Despite the retrospective nature of the analyses, the results demonstrated the robustness of the suprachoroidal injection regardless of indications. The two needle length options successfully accommodate for anatomical variations across patients.
Presentation: https://learning.arvo.org/diweb/catalog/launch/media/eid/5252042
Abstract: https://iovs.arvojournals.org/article.aspx?articleid=2769429&resultClick=1

Macular Edema

Title: Best Corrected Visual Acuity and Central Subfield Thickness in Macular Edema Due to Retinal Vein Occlusion, Diabetic Retinopathy and Noninfectious Uveitis
Authors: Dilraj Grewal; Thomas A Ciulla; Barry Kapik
Conclusions: In this cohort of over 1000 eyes, there were moderate relationships between BCVA and central subfield thickness (CST) in patients with ME due to RVO, diabetic macular edema (DME) and noninfectious uveitis at baseline and these were similar across disease states. There were also moderate relationships between BCVA and CST across these disease states with respect to change from baseline to 6 months. These correlations provide context around the use of CST in clinical decision making and visual recovery.

Presentation: https://learning.arvo.org/diweb/catalog/item?id=5255154
Abstract: https://iovs.arvojournals.org/article.aspx?articleid=2767953&resultClick=1

Title: Results from the Phase 3 PEACTHREE Clinical Trial: Efficacy of CLS-TA in Patients Not Taking Systemic Therapy, a Post-Hoc Analysis
Authors: Christopher R Henry; Thomas Ciulla; Colette Hall
Conclusions : These post hoc results corroborate the prespecified study analyses in the PEACHTREE trial. With respect to BCVA and CST, a clinically meaningful relative benefit of CLS-TA over control was noted in patients on systemic immunosuppression as well as those not on other systemic therapies.
Presentation: https://learning.arvo.org/diweb/catalog/launch/media/eid/5229294
Abstract: https://iovs.arvojournals.org/article.aspx?articleid=2769192&resultClick=1

Title: Area of Disorganization of the Retinal Inner Layers (DRIL) as a Quantitative Biomarker in Eyes with Diabetic Macular Edema
Authors: Swetha Bindu Velaga; Muneeswar Gupta Nittala; Jyotsna Maram; Thomas A Ciulla; Michael S Ip; Srinivas Sadda
Conclusions : The extent of DRIL appears to decrease following treatment of DME. Area of DRIL correlates better with visual function than the linear extent of DRIL, and may be a useful quantitative biomarker in future studies of diabetic macular edema.
Abstract: https://iovs.arvojournals.org/article.aspx?articleid=2768726&resultClick=1

Copies of these presentations will also be available on Clearside's website under the Publications & Presentations page here: 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 this proprietary suspension of axitinib has demonstrated meaningful potential in preclinical studies in multiple species. Preclinical results from Clearside and outside investigators showed pharmacodynamic effect 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.

About Clearside's Suprachoroidal Space (SCS) Injection Platform

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 medications, new formulations of medicines, as well as future innovations such as gene therapy.

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 the development and potential benefits of CLS-AX and the SCS Microinjector and the timeline for submitting the IND 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, 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, 2019, filed with the U.S. Securities and Exchange Commission ("SEC") on March 13, 2020, Clearside's Quarterly Report on Form 10-Q filed with the SEC on May 8, 2020 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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