Clearside Biomedical Announces Plans for ODYSSEY Phase 2b Clinical Trial of CLS-AX (axitinib injectable suspension) in Wet AMD

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- Multiple U.S. Clinical Sites to Begin Enrolling ODYSSEY Participants This Quarter -

- ODYSSEY Topline Results Expected in Q3 2024 -

ALPHARETTA, Ga., April 18, 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 plans for ODYSSEY, a randomized, double-masked, parallel-group, active-controlled, multi-center Phase 2b clinical trial of CLS-AX (axitinib injectable suspension) using suprachoroidal delivery in neovascular age-related macular degeneration (wet AMD). The Company plans to open the trial for enrollment this quarter and expects topline results in Q3 2024.

George Lasezkay, Pharm.D., J.D., Clearside's President and Chief Executive Officer, commented, "We are excited to advance our CLS-AX program, building on the positive data from our OASIS Phase 1/2a trial, which showed that CLS-AX was well tolerated and demonstrated an excellent safety profile and promising data up to 6 months durability. We believe CLS-AX has the potential to reduce treatment burden in patients with wet AMD while maintaining visual acuity."

"We are actively preparing to open enrollment in ODYSSEY at multiple U.S. clinical trial sites this quarter. Based on the recent draft guidance on wet AMD drug development from the U.S. Food & Drug Administration, we believe that our team has optimized the trial design to efficiently provide the necessary data to design the Phase 3 program. ODYSSEY will enroll treatment-experienced participants with wet AMD and use aflibercept, a current standard of care, as the comparator, over 36 weeks of treatment. We expect ODYSSEY topline results in Q3 2024," concluded Dr. Lasezkay.

About the ODYSSEY Phase 2b Clinical Trial

ODYSSEY is a randomized, double-masked, parallel-group, active-controlled, multi-center, Phase 2b clinical trial of 36 weeks duration.

- Number of Participants: 60 total participants with 2:1 randomization.
  - 40 participants in CLS-AX arm and 20 participants in aflibercept arm.
- Key inclusion criteria:
  - Diagnosed with wet AMD within 36 months of screening.
  - History of 2 to 4 anti-VEGF treatments in the 6 months before screening.
  - History of response to anti-VEGF treatment for wet AMD.
  - Reading center confirmation of persistent active disease.
  - Best corrected visual acuity (BCVA) of 20 to 80 letters
- Loading Doses: Participants in both arms will receive 3 aflibercept (2 mg) loading doses. In the CLS-AX arm, participants will receive one dose of CLS-AX (1.0 mg) at the same visit as the second loading dose of aflibercept (Baseline).
- Treatments:
  - In the CLS-AX arm, following the 3 loading doses of aflibercept and the initial dose of CLS-AX at Baseline, participants will receive CLS-AX at least every 24 weeks unless more frequently required based on disease activity.
  - In the aflibercept arm, following the 3 loading doses, participants will receive aflibercept on a fixed dosing regimen every 8 weeks.
- Monthly disease activity assessments: Will be conducted in both arms at Weeks 12 through 32 to determine if there is a need for supplemental treatment.
- Supplemental treatment criteria (based on measurement changes due to wet AMD):
  - BCVA reduction of >10 letters from Baseline.
  - Increase in central subfield thickness (CST) of >100 microns on SD-OCT from Baseline.
  - BCVA reduction of > 5 letters from Baseline AND increase in CST of >75 microns on SD-OCT from Baseline.
  - Presence of new or worsening vision-threatening hemorrhage.
- Primary outcome measure: Mean change in BCVA from Baseline to Week 36.
- Secondary outcome measures:
  - Other changes in visual function and ocular anatomy, such as CST.
  - Need for supplemental treatment.
  - Treatment burden as measured by total injections over trial duration.

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 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, there is the potential to achieve prolonged duration and targeted delivery to affected tissue layers while limiting exposure of drug to the front of the eye. 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 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'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 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 of CLS-AX, the timeline for initiating the ODYSSEY Phase 2b clinical trial for CLS-AX, the expected timing of topline results from the ODYSSEY clinical trial and the potential benefits of 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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