Kodiak Sciences Announces Topline Results from its Phase 3 Studies of Tarcocimab Tedromer in Neovascular Age-Related Macular Degeneration and Diabetic Macular Edema and Provides Update on Tarcocimab Development Program

July 24, 2023 at 6:00 AM EDT

PALO ALTO, Calif., July 24, 2023 /PRNewswire/ -- Kodiak Sciences Inc. (NASDAQ: KOD) announced today topline results from three Phase 3 studies of tarcocimab tedromer, a novel antibody biopolymer conjugate.

The DAYLIGHT study was a randomized, double-masked, active comparator-controlled study evaluating the efficacy and safety of a high intensity dosing regimen of tarcocimab tedromer in 557 treatment-naïve subjects with wet AMD. The DAYLIGHT study met the primary endpoint of non-inferior visual acuity gains for tarcocimab dosed monthly compared to aflibercept dosed every 8 weeks following 3 monthly loading doses. Tarcocimab was safe and well tolerated in the study and with a low rate of intraocular inflammation.

The GLEAM and GLIMMER studies are identically designed, randomized, double-masked, active comparator-controlled studies evaluating the efficacy, durability and safety of tarcocimab tedromer in 460 and 457 treatment-naïve subjects with DME, respectively. Although high proportions of patients on meaningfully longer treatment intervals were observed with tarcocimab, with half of patients on every 24-week dosing at the primary endpoint, the GLEAM and GLIMMER studies did not meet their primary efficacy endpoints of showing non-inferior visual acuity gains for tarcocimab dosed every 8 to 24 weeks after 3 monthly loading doses compared to aflibercept given every 8 weeks after 5 monthly loading doses. An unexpected increase in cataracts was observed over time in the tarcocimab arms of both GLEAM and GLIMMER, and Kodiak's initial evaluation suggests that this contributed meaningfully to the failure of each study. In the DAYLIGHT study, no imbalance in cataracts was observed between wet AMD patients receiving tarcocimab or aflibercept throughout the one-year study period despite the intensive monthly tarcocimab dosing regimen.

Based on these data, and despite demonstrating great potential, Kodiak has made a business decision to discontinue further development of tarcocimab.

"A successful efficacy, durability and safety outcome in both GLEAM and GLIMMER was the basis of our regulatory and clinical development strategy for tarcocimab," said Victor Perlroth, MD, Kodiak's Chief Executive Officer, in explaining the decision. "After our unsuccessful Phase 2b study in wet AMD last year, we made a number of changes to the GLEAM and GLIMMER study design to increase their probability of success, and we saw the positive impact of those changes in the GLEAM and GLIMMER data. Notably, the conjugate delivered on the promise of early potency and strong consistent durability through the study. After getting these results, the immediate question is why did the GLEAM and GLIMMER studies fail?"

"We have gained three main insights from the initial data analysis. First, through the matched three loading doses, vision and anatomic improvements were strong and comparable between tarcocimab and aflibercept. Second, in a subset of patients to be determined, additional loading doses with tarcocimab might have helped better achieve early disease control to set an even higher visual acuity base entering into the dose interval adjustment phase, but the overall effect of this was not a primary driver of study failure. Third, and most critically, an unforeseen imbalance in cataract adverse events emerged in the last third of the study (19% of patients on tarcocimab versus 9% of patients on aflibercept by the primary endpoint), and we believe this likely was the primary driver for tarcocimab failing to achieve BCVA non-inferiority to aflibercept in these studies. A sub-analysis of the pseudophakic patients (who enter the study having already had cataract surgery) and who represented 25% of the total study population supports this view as does initial analysis of the OCT anatomic data from the two studies. The development of cataracts did not appear to correlate with the timing or number of tarcocimab doses patients had received. Importantly, in the DAYLIGHT study which explored a maximal, monthly regimen of tarcocimab 5mg in wet AMD patients, a median of 12 tarcocimab doses were given over one year and patients experienced fewer events of cataract on tarcocimab than on aflibercept (3% versus 5%). Thus, what drove the increased incidence of cataracts with tarcocimab in DME remains unclear at this time. Given these findings and results, we are discontinuing development of the tarcocimab program," concluded Dr. Perlroth.

"While vision improvements were more closely matched in the first two-thirds of each study, at the primary efficacy endpoint of the GLEAM study patients treated with tarcocimab gained an average of 6.4 eye chart letters (to 73.1 letters) compared with 10.3 letters for patients treated with aflibercept (to 76.5 letters)," said Jason Ehrlich, MD, PhD, Kodiak's Chief Medical Officer. "In GLIMMER, patients treated with tarcocimab gained an average of 7.4 eye chart letters at the primary endpoint (to 72.5 letters) compared with 12.2 letters (to 76.4 letters) for patients treated with aflibercept. Half of tarcocimab treated patients were on every 6-month dosing at the primary endpoint, two-thirds achieved at least one 6-month dosing interval during the studies, and three-quarters achieved at least one 5-month or longer treatment interval. Aside from the increase in cataracts, no new or unexpected safety signals were identified in GLEAM and GLIMMER. Intraocular inflammation was rare, occurring in 1.3% and 0.2% of tarcocimab and aflibercept treated patients, respectively. No cases of intraocular inflammation with vasculitis or vascular occlusion were observed. In the DAYLIGHT study, intraocular inflammation occurred in 3.3% of patients treated with monthly tarcocimab and 0.4% of patients treated with aflibercept, again with no vasculitis or occlusion."

"We sincerely thank the participants, clinicians and site staff who participated in the tarcocimab clinical trials and who continue to participate in the ongoing clinical program of our second investigational medicine, KSI-501," said Drs. Perlroth and Ehrlich. "We are also especially grateful to all of the Kodiak team members and our partners who are dedicated to developing novel therapeutics for eye diseases and have made these projects possible."

Dr. Perlroth continued, "Kodiak remains well financed with approximately $379 million cash and cash equivalents as of June 30, 2023 (unaudited) providing us with significant optionality following the wind-down of the tarcocimab program. We will be assessing our capabilities and the many learnings gained by Kodiak during the development of tarcocimab as we reset our near-term plan."

"While we have not come to a final conclusion, we remain committed to our vision and mission of developing transformative therapies for high prevalence diseases. In this regard, we believe our KSI-501 program has a differentiated mechanism of action targeting both IL-6 mediated immune-inflammation as well as VEGF mediated angiogenesis and vascular permeability. The KSI-501 clinical program is underway with enrollment in the Phase 1 multiple dose escalation study nearly complete. In light of the emergence of late onset cataracts observed with tarcocimab in GLEAM and GLIMMER but not DAYLIGHT, we are assessing whether to continue development of KSI-501 both as (i) its unconjugated protein which is itself a

novel bispecific anti-IL-6 antibody / anti-VEGF trap fusion protein and (ii) its bioconjugate form. In this manner, we would continue development of this novel retina program while decreasing our reliance on the ABC platform, thus allowing a more thorough exploration of platform versus product profiles. Meanwhile, we look forward to advancing our triplet platform and other protein therapeutic and small molecule programs. Our triplet platform is designed to enable multi-mechanism targeting of multifactorial diseases by embedding small molecules in the biopolymer backbone to provide a high drug-antibody ratio (DAR). The small molecules can be released over time to achieve sustained inhibition of targeted biological pathways. We plan to explore the utility of this unique combination of high DAR and extended therapeutic benefit in retinal and systemic diseases."

"In summary, we are deeply disappointed with the GLEAM and GLIMMER outcome. We recognize the risks inherent to innovative drug development and expect to continue to work towards the goal of translating our capabilities and substantive cash position into value for our stakeholders."

Detailed results of the GLEAM and GLIMMER studies are scheduled to be presented by study investigator Dr. Charles C. Wykoff, MD, PhD, as a late-breaking presentation at the 41st Annual Scientific Meeting of the American Society of Retina Specialists, which will be held beginning next week in Seattle, WA. The presentation is currently scheduled for Sunday, July 30, 2023 at 3:51pm Pacific Time. A copy of the slides will be made available on the Kodiak Investor Relations website.

It is anticipated that data from the DAYLIGHT study and additional results and insights from the tarcocimab development program, such as the pending BEACON study year one data in retinal vein occlusion and pending topline results of the GLOW study in non-proliferative diabetic retinopathy, will be presented at upcoming medical conferences.

About the GLEAM and GLIMMER Studies

The GLEAM and GLIMMER studies together randomized 919 patients into two treatment arms: tarcocimab 5 mg or aflibercept 2 mg. Tarcocimab was dosed every 8, 12, 16, 20 or 24 weeks following 3 monthly loading doses. Aflibercept was dosed as per its label, on a fixed every 8-week interval following 5 monthly loading doses. Subjects on tarcocimab were assessed 8 weeks after the completion of their loading phase and, based on predefined disease activity criteria, were assigned to a base treatment interval of every 8 to 24 weeks. Patients were evaluated monthly thereafter, and treatment intervals were extended, maintained or reduced based on disease activity. The primary endpoint of the study was the average change in best-corrected visual acuity (BCVA) score (a measure of the best vision a person can achieve when reading letters on an eye chart, including with correction such as glasses) from baseline averaged over weeks 60 and 64. For the assessment of the primary efficacy endpoint, the BCVA of tarcocimab patients in all dosing intervals was compared as a single group to the aflibercept group dosed every 8 weeks. Additional information about GLEAM (also called Study KS301P104) and GLIMMER (also called Study KS301P105) can be found on www.clinicaltrials.gov under Trial Identifiers NCT04611152 and NCT04603937, respectively (https://clinicaltrials.gov/ct2/show/NCT04611152 and https://clinicaltrials.gov/ct2/show/NCT04603937).

About the DAYLIGHT Study

The Phase 3 DAYLIGHT study is a global, multi-center, randomized pivotal study designed to evaluate the efficacy and safety of high-frequency tarcocimab in patients with treatment-naïve wet age-related macular degeneration (wet "AMD"). The DAYLIGHT study randomized 557 patients to receive either tarcocimab on a monthly dosing regimen or to receive aflibercept on a fixed dosing regimen of every 8-weeks after three monthly loading doses per its label. The primary endpoint is at year one. The DAYLIGHT study is intended to evaluate the safety and efficacy of tarcocimab in treating high need patients with wet AMD. Additional information about DAYLIGHT (also called Study KS301P107) can be found on www.clinicaltrials.gov under Trial Identifier NCT04964089 (https://clinicaltrials.gov/show/NCT04964089).

About KSI-501

KSI-501 is a first-in-class bispecific investigational medicine designed to inhibit two mechanisms implicated in retinal diseases: interleukin-6 (IL-6) and vascular endothelial growth factor ("VEGF"). IL-6 is a pro-inflammatory cytokine and growth factor implicated in the pathophysiology of multiple retinal diseases and, in conditions for which anti-VEGF treatment is used, elevated levels of ocular IL-6 have been associated with poor anti-VEGF treatment response. KSI-501 is a trap-antibody fusion biopolymer conjugate designed to provide potent inhibition of (i) VEGF-mediated angiogenesis and vascular permeability through a soluble decoy receptor inhibiting the binding of VEGF-A and PLGF to their cognate receptors and (ii) IL-6 mediated inflammation through an antibody that binds soluble interleukin-6, inhibiting its binding to both soluble and membrane-bound IL-6 receptors. In cell-based assays, KSI-501 inhibits angiogenesis and also normalizes inner and outer blood retinal barriers; dual inhibition of VEGF and IL-6 by KSI-501 confers superior normalization of cell morphology and junctional biology compared to either anti-VEGF or anti-IL-6 monotherapy. We believe KSI-501 has the potential to become a new category of retinal medicines with greater therapeutic utility than existing therapies. A Phase 1 study of KSI-501 is currently dosing patients in the United States to evaluate the safety, tolerability and bioactivity of KSI-501 in patients with DME.

About Kodiak Sciences Inc.

Kodiak (Nasdaq: KOD) is a biopharmaceutical company committed to researching, developing and commercializing transformative therapeutics to treat high prevalence retinal diseases. We are focused on bringing new science to the design and manufacture of next generation retinal medicines to prevent and treat the leading causes of blindness globally. KSI-501 is Kodiak's first-in-class bispecific investigational medicine targeting both IL-6 (anti-IL-6 antibody) and VEGF (VEGF-trap) and is being investigated in a Phase 1 clinical study initially in patients with diabetic macular edema. We are expanding our early research pipeline to include ABC Platform based triplet inhibitors for multifactorial diseases. Kodiak is based in Palo Alto, CA. For more information, please visit www.kodiak.com.

Forward-Looking Statements

This release contains "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933, Section 21E of the Securities Exchange Act of 1934 and the Private Securities Litigation Reform Act of 1995. These forward-looking statements are not based on historical fact and include statements regarding: the realignment of our priorities after tarcocimab clinical study readouts; and potential expansion of our research pipeline. Forward-looking statements generally include statements that are predictive in nature and depend upon or refer to future events or conditions, and include words such as "may," "will," "should," "would," "could," "expect," "plan," "believe," "intend," "pursue," and other similar expressions among others. Any forward-looking statements are based on management's current expectations of future events and are subject to a

number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in or implied by such forward-looking statements. These risks and uncertainties include, but are not limited to: the risk that cessation or delay of any of the ongoing clinical studies and our development of KSI-501 may occur; the risk that preliminary safety, efficacy and durability data for our product candidates may not continue or persist; our research and development efforts and our ability to advance our product candidates into later stages of development may fail; the risk that any one or more of our product candidates may not be successfully developed, approved or commercialized; adverse conditions in the general domestic and global economic markets, which may significantly impact our business and operations, including our clinical trial sites, as well as the business or operations of our manufacturers, contract research organizations or other third parties with whom we conduct business; as well as the other risks identified in our filings with the Securities and Exchange Commission. In addition, the Company's unaudited cash and cash equivalents as of June 30, 2023 is subject to revision based upon the Company's quarter-end closing procedures and the completion and external review of the Company's financial statements as of and for the quarter ended June 30, 2023. For a discussion of other risks and uncertainties, and other important factors, any of which could cause our actual results to differ from those contained in the forward-looking statements, see the section entitled "Risk Factors" in our most recent Form 10-K, as well as discussions of potential risks, uncertainties, and other important factors in our subsequent filings with the Securities and Exchange Commission. These forward-looking statements speak only as of the date hereof and Kodiak undertakes no obligation to update forward-looking statements, and readers are cautioned not to place undue reliance on such forward-looking statements. Kodiak®, Kodiak Sciences®, ABC™, ABC Platform™ and the Kodiak logo are registered trademarks or trademarks of Kodiak Sciences Inc. in various global jurisdictions.

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