# Kodiak Sciences Announces First Patients Enrolled in Global Phase 3 ALTO trial of KSI-501 in Patients with Diabetic Macular Edema

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- *Phase 3 ALTO trial designed to demonstrate superiority of KSI-501 versus aflibercept in patients with diabetic macular edema*

PALO ALTO, Calif., Aug. 10, 2026 /PRNewswire/ -- Kodiak Sciences Inc. (Nasdaq: KOD), a precommercial retina-focused biotechnology company committed to researching, developing and commercializing transformative therapeutics, today announced that the first patients have been enrolled in the global Phase 3 ALTO trial evaluating KSI-501 in patients with diabetic macular edema (DME). KSI-501 is an investigational, first-in-class bispecific therapy built on Kodiak's ABC® Platform and designed to potently inhibit two complementary pathways implicated in retinal vascular disease: interleukin (IL)-6-mediated inflammation and vascular endothelial growth factor (VEGF)-mediated vascular permeability and neovascularization.

The ALTO trial is designed to demonstrate the superiority of bispecific (anti-VEGF, anti-IL-6) KSI-501 versus monospecific (anti-VEGF) aflibercept in patients with DME. ALTO is the second registrational Phase 3 trial of KSI-501, following the DAYBREAK study in patients with wet AMD.

ALTO explores whether dual inhibition of immune and vascular pathways can deliver deeper and more sustained disease control for patients with DME and evaluates two dosing regimens, one regimen with intensive dosing and a second regimen with individualized dosing intervals of up to every six months.

"Initiating ALTO is an important next step for KSI-501 and for our broader effort to advance multifunctional retinal medicines that address disease biology beyond VEGF alone," said Victor Perlroth, M.D., Chief Executive Officer of Kodiak. "Anti-VEGF therapies have transformed the treatment of DME, yet many patients continue to live with persistent retinal fluid, incomplete visual recovery and the burden of frequent ongoing injections. We believe that inhibiting the immune-focused IL-6 pathway alongside the vessel-focused VEGF pathway, further enhanced with the durability of our ABC Platform, may achieve deeper and more sustained control of this disease."

"It has long been believed that there is more to be gained for patients with DME by targeting mechanisms beyond VEGF, and in particular by addressing the chronic, low-grade inflammatory state that often persists in patients who have suboptimal response to anti-VEGF monotherapy," said Margaret Chang, M.D., M.S., Co-Director of Clinical Research at Retina Consultants Medical Group. "Recent results from the Phase 2 ALLUVIUM study demonstrated that IL-6 inhibition alone can lead to clinically meaningful functional and anatomic benefits in DME patients, providing evidence that the IL-6 pathway is biologically active in diabetic eye diseases and operates independently of VEGF-driven pathology. Importantly, the recent Phase 2 BARDENAS study further suggested that dual inhibition of VEGF and IL-6 may offer synergistic effects, with the potential to deliver superior vision gains and improved fluid control versus targeting either pathway alone."

"DME is a multifactorial disease in which vascular leakage, blood-retinal barrier dysfunction and immune signaling together drive retinal edema and vision loss," said J. Pablo Velazquez-Martin, M.D., Chief Medical Officer of Kodiak. "Our ALTO study is designed to rigorously evaluate whether dual inhibition of IL-6 and VEGF translates into meaningful benefit for patients, including the potential for better vision gains and greater fluid control, and through Kodiak's ABC biopolymer conjugate platform the potential for superior durability. Alongside the primary visual acuity endpoint, the study is powered for a key secondary endpoint of two-step or greater improvement on the Diabetic Retinopathy Severity Scale (DRSS), and it evaluates a regimen with dosing intervals extending to six months. Our objective is to characterize efficacy, anatomic response and durability in a single Phase 3 program."

**About the ALTO Study**

The ALTO Study (KSMP002-S1) is a global, multicenter, randomized, double-masked, active comparator-controlled Phase 3 study evaluating the efficacy and safety of intravitreal KSI-501 5 mg compared with intravitreal aflibercept 2 mg in patients with visual impairment secondary to center-involved DME.

Approximately 910 patients, treatment-naïve or previously treated, will be randomized 5:3:5 to one of three arms:

- **Arm A:** KSI-501 5 mg every 8 weeks, with monthly assessment for additional individualized dosing, following six monthly loading doses
- **Arm B:** KSI-501 5 mg on an individualized regimen of every 4 to 24 weeks, following six monthly loading doses
- **Arm C:** aflibercept 2 mg every 8 weeks, following five monthly loading doses

The primary endpoint is the mean change in best-corrected visual acuity from baseline to the average of Week 48 and Week 52. The key secondary endpoint is the proportion of patients improving two or more steps on the DRSS from baseline at Week 48. Additional secondary and exploratory endpoints evaluate visual function, retinal anatomy, treatment burden and durability, and safety.

Participants will be treated and followed for approximately 96 weeks. Additional information about ALTO, also known as Study KSMP002-S1, is available at https://clinicaltrials.gov/study/NCT07734844.

**The Potential of Dual IL-6 and VEGF Inhibition in DME**

VEGF is an established driver of vascular permeability and abnormal vessel growth in retinal vascular disease, and anti-VEGF therapy has revolutionized the treatment of DME by reducing retinal fluid and delivering meaningful vision gains for the majority of patients. Yet significant room for improvement remains. Across pivotal DME trials, a substantial proportion of patients have persistent edema despite ongoing treatment, and most patients do not achieve 20/20 vision. While recent intravitreal biologics have extended dosing intervals, many patients still require frequent injections to

sustain their best possible visual outcome.

IL-6 is a pro-inflammatory cytokine and immune growth factor implicated in inflammatory signaling, endothelial dysfunction and disruption of the blood-retinal barrier. Ocular IL-6 is elevated in patients with DME, and higher intraocular IL-6 levels have been associated with poorer visual outcomes in patients treated with anti-VEGF monotherapy.

KSI-501 is designed to address these complementary mechanisms in a single intravitreal medicine. The VEGF-trap component mimics the native VEGF receptors and is designed to inhibit VEGF-mediated vascular permeability and neovascularization. The anti-IL-6 antibody component is designed to inhibit IL-6-mediated inflammatory signaling and normalize the blood-retinal barrier. The ABC Platform-based design, with its signature 20-day intraocular half-life, is intended to support sustained intraocular activity and extended durability.

In preclinical models, KSI-501 was shown to be a potent inhibitor of both VEGF and IL-6 and to normalize the blood-retinal barrier, opening the possibility that KSI-501 may be a disease-modifying therapy for retinal vascular diseases.

**About KSI-501**

KSI-501 is an investigational anti-IL-6, VEGF-trap bispecific therapy built on the ABC platform and is being developed for high prevalence retinal vascular diseases to address the leading unmet needs of extended durability and targeting disease biology beyond VEGF for differentiated efficacy. KSI-501 is designed to provide high immediacy/efficacy, driven by the enhanced formulation, and high durability, driven by the ABC platform and our science of durability.

Kodiak has advanced KSI-501 into the registrational Phase 3 study DAYBREAK to evaluate its efficacy and safety in wet AMD. DAYBREAK uses KSI-501's enhanced 50 mg/mL formulation containing both conjugated and unconjugated antibody that is intended to balance immediacy and durability. DAYBREAK has completed enrollment. Topline data for the one-year primary endpoint in DAYBREAK are expected in September 2026.

Kodiak has also advanced KSI-501 into the registrational Phase 3 ALTO study designed to demonstrate the superiority of bispecific KSI-501 (anti-VEGF, anti-IL-6) versus monospecific aflibercept (anti-VEGF) in patients with diabetic macular edema. The ALTO study is now enrolling patients.

**About Kodiak Sciences Inc.**

Kodiak Sciences (Nasdaq: KOD) is a pre-commercial retina-focused biotechnology company committed to researching, developing and commercializing transformative therapeutics. 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. We are developing a portfolio of three late-stage clinical programs. Zenkuda™ (tarcocimab tedromer) has a BLA-ready profile in diabetic retinopathy, retinal vein occlusion and wet AMD, and, together with KSI-501, is being explored in the BLA-facing Phase 3 DAYBREAK wet AMD study, with topline data expected in September 2026. Zenkuda and KSI-501 target the $15 billion anti-VEGF market across retinal vascular diseases. KSI-101 is a bispecific protein being explored in two BLA-facing Phase 3 studies in Macular Edema Secondary to Inflammation (MESI). Topline data for Pivotal Analysis 1 (PEAK) are expected in December 2026 and Pivotal Analysis 2 (PEAK+PINNACLE) in 2Q 2027.

**Forward-Looking Statements**

This press 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, but are not limited to, statements regarding: the ability to demonstrate the superiority of KSI-501 over aflibercept in patients with DME; the potential for dual inhibition of the IL-6 and VEGF pathways to deliver deeper and more sustained disease control for patients with DME; the possibility that KSI-501 may be a disease-modifying therapy for retinal vascular diseases. 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," "anticipate," 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 the Phase 3 ALTO trial may not achieve its primary or key secondary endpoints or may not do so on the anticipated timeline; the risk that dual inhibition of IL-6 and VEGF may not translate into the clinical benefits observed or suggested in earlier studies, including the Phase 2 ALLUVIUM and BARDENAS studies; as well as the other risks identified in the section entitled "Risk Factors" in Kodiak's most recent Annual Report on Form 10-K, as well as discussions of potential risks, uncertainties, and other important factors in Kodiak's subsequent filings with the Securities and Exchange Commission. These forward-looking statements speak only as of the date of this press release, and Kodiak undertakes no obligation to update or revise any forward-looking statements, whether as a result of new information, future events, or otherwise. Readers are cautioned not to place undue reliance on such forward-looking statements.

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