



## Article:

# ADVANCING VISION: TRENDS AND BREAKTHROUGHS IN THE WET & DRY AMD CLINICAL TRIAL LANDSCAPE

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Age related macular degeneration (AMD) is approached strategically in clinical trials based on whether disease progression is driven by abnormal blood vessel growth (wet AMD) or gradual retinal cell loss and atrophy (dry AMD).

While anti-VEGF therapy remains foundational in wet AMD, research efforts aim to extend durability by introducing long-acting biologics, sustained-delivery systems, and gene therapies that only require single interventions.<sup>1,2</sup> The current therapeutic landscape for dry AMD focuses on addressing key pathologic mechanisms targeted at slowing disease progression and preserving retinal function. Modalities such as oral medications, subcutaneous injections, and eye drops offer less invasive and more convenient dosing, therefore improving compliance and broadening access to treatment.<sup>3</sup> Gene therapy and stem cell injections, while more intensive procedurally, provide a more durable option that may eliminate repeat dosing.<sup>4</sup>

With both Wet and Dry AMD characterized by distinct pathophysiology yet overlapping unmet needs, the current clinical trial landscape reflects a growing diversification of therapeutic strategies. As innovation accelerates across modalities, targets, and delivery approaches, understanding where development efforts are more concentrated provides critical insight into the future direction of AMD treatment.

## AMD PIPELINE AT A GLANCE: WHERE INNOVATION IS CONCENTRATED

The main focus of treatment for wet AMD remains through extracellular VEGF pathways.<sup>5</sup> Other categories target integrin, TIE2 activation, or WNT pathways, allowing for the development of combination or alternative therapies using biologics, small molecules, or gene therapy to improve efficacy and durability in wet AMD.<sup>6</sup> Therapeutic approaches for dry AMD can be classified according to their underlying mechanism. Current research focuses on strategies to lower oxidative stress, reduce toxic byproducts such as beta-amyloid oligomers, modulate the visual cycle, inhibit the complement system, and regulate active inflammasomes.<sup>7</sup>

From our perspective as a CRO, the execution of AMD trials is fundamentally redefined by a shift toward therapeutic “durability” and the integration of multimodal imaging as a primary driver of data integrity. In wet AMD, we are seeing a transition from traditional anti-VEGF injections to gene therapies and sustained-release systems, which require specialized site training to manage complex administration and “masking” protocols. For dry AMD, the focus has shifted toward earlier intervention and disease-modifying goals, particularly in managing Geographic Atrophy (GA).

To address the increasing role of biomarkers, we leverage our established partnerships with imaging vendors. By working with the central imaging reader to qualify specialized equipment and imaging technicians, we aim to ensure consistency across all study sites. We ensure that qualification images—such as Optical Coherence Tomography (OCT) and Fundus Autofluorescence (FAF)—are captured and transferred with high precision prior to activating a site for study recruitment. We partner with imaging readers that are well respected in the industry and have established relationships with our study sites as well.

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## DIFFERENTIATION IN A CROWDED FIELD: WHAT SEPARATES MEDPACE

In the highly competitive AMD landscape, the difference between a successful program and a stalled one often lies in enrollment feasibility and the mitigation of site burden. We differentiate ourselves through internal performance metrics from our extensive global database to selecting high-performing sites with proven track records in AMD recruitment. This is critical as we navigate a landscape where multiple trials compete for the same patient pool. Our specialized **Site Activation and Maintenance (SAM)** team ensures that we leverage existing relationships with key opinion leaders (KOLs) and networks to expedite start-up. In combination with providing support to complete study start-up requirements, including completion of site essential documents, regulatory submissions/approval, and site training requirements Medpace achieves “First Patient First Visit” faster than industry averages.

Our operational excellence is further reinforced by our embedded medical leadership, featuring board-certified ophthalmologists who provide real-time medical monitoring and safety surveillance. To enhance the patient experience—a major factor in long-term AMD studies—we deploy **Medpace Patient Concierge Services (PCS)** to manage travel logistics and minimize the burden on elderly or visually impaired participants. Furthermore, our use of the **TrialPACE®** app allows patients to complete ePROs and diaries from home, significantly reducing the frequency of in-person clinic visits and improving overall retention rates.

## WHAT'S NEXT: THE FUTURE OF AMD DEVELOPMENT

Regulatory expectations are increasingly shaping development strategies for wet and dry AMD. While functional outcomes, such as changes in best-corrected visual acuity, are prioritized by the U.S. Food and Drug Administration (FDA) in wet AMD, they have recently accepted more imaging-based endpoints such as ellipsoid zone data and lesion growth size. Medpace continues to work with reading centers to ensure accurate and timely imaging data. This drives development programs toward large, randomized trials to demonstrate non-inferiority, superiority, or improved durability compared with approved anti-VEGF treatments.<sup>2,8</sup> In dry AMD, regulators have demonstrated flexibility, reflecting the lack of sensitive functional endpoints and unmet medical need by accepting<sup>3</sup> endpoints, such as rate of lesion growth measured by fundus autofluorescence.<sup>9</sup>

## CONCLUSION

Clinical trial complexity in both wet and dry AMD is increasing due to evolving therapies, regulatory expectations, and the need for more sensitive endpoints. Trials are moving beyond traditional visual acuity and retinal thickness measures to incorporate multimodal imaging, fluid dynamics, and durability assessments. Additional operational and statistical complexity is added to dry AMD trials, which often require longer follow-up to detect meaningful changes by using structural imaging endpoints, functional assessments, and patient-reported outcomes.

Partnering with an experienced ophthalmology CRO supports complex wet and dry AMD trials by combining operational expertise, medical leadership, and regulatory guidance. Medpace's experience with complex trial designs helps optimize efficiency, data integrity, and regulatory success. Embedded board-certified ophthalmologists provide continuous safety oversight, managing adverse events, and ensuring protocol adherence in a field that continues to rapidly evolve.



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## FULL-SERVICE CLINICAL DEVELOPMENT

Medpace is a scientifically-driven, global, full-service clinical contract research organization (CRO) providing Phase I-IV clinical development services to the biotechnology, pharmaceutical and medical device industries. Medpace's mission is to accelerate the global development of safe and effective medical therapeutics through its high-science and disciplined operating approach that leverages local regulatory and deep therapeutic expertise across all major areas including oncology, cardiology, metabolic disease, endocrinology, central nervous system and anti-viral and anti-infective.

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