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## AGENTS UNDER STUDY

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The advent of intravitreal anti-vascular endothelial growth factor (VEGF) therapy has undoubtedly revolutionized the field of ophthalmology and how physicians manage many potentially debilitating retinal conditions. In the recently published 5-year outcomes with anti-VEGF therapy from the Comparison of Age-Related Macular Degeneration Treatment Trials, a remarkable 50% of follow-up participants had visual acuity of 20/40 or better; however, 20% of individuals had acuity of 20/200 or worse.<sup>1</sup> While this represents a significant improvement over previous natural history studies prior to the commencement of the anti-VEGF era, it is a reminder that much work remains to be accomplished.

In an effort to reduce the overall treatment burden of serial anti-VEGF injections on retinal specialists, patients, caregivers, and society at large, numerous targeted therapies are under investigation to further improve patient outcomes and decrease overall costs of treatment to the health care system. This chapter will serve to summarize some of the most pertinent programs in development, and is broken down based on the different routes of drug delivery: gene therapy, intravitreal injections, systemic therapy, and topical treatment.

### Gene Therapy

The goal of gene therapy is to provide continual expression of a protein(s) of interest involved in the pathogenesis of a disease for sustained therapeutic benefit. Gene therapy for retinal degenerative diseases is a field receiving significant research and developmental focus recently, as a number of therapies are progressing to human clinical trials. In these individuals, a viral vector is used to carry the desired genetic information encoding a protein(s) of interest into the target cells. Successfully transduced vectors then use the host cell's machinery to express the particular protein(s). Two main categories of vectors are being investigated: integrating vectors and nonintegrating vectors. Integrating