



'Targeting the diseased tissue to restore normal function is a fundamental tenet of medicine, yet no available glaucoma therapies do this.

We founded Aerie with the specific goal of bringing a safe and effective trabecular outflow drug to physicians and their patients.'<sup>1</sup>

-Dr. David Epstein (1943-2014) Former Duke University Chairman of the Department of Ophthalmology and Aerie Co-founder

Aerie began in 2005 after David Epstein, MD; Erik Toone, PhD; and Casey C. Kopczynski, PhD joined forces.<sup>1</sup> Dr. Epstein, then Chairman of the Department of Ophthalmology at Duke University, was a long-time clinical scientist in the glaucoma field. He spent his research career searching for better ways to treat glaucoma, the disease that causes irreversible vision loss. Dr. Epstein collaborated with chemists to translate compound structures into clinical medications.<sup>2</sup> Dr. Kopczynski, a biotech start-up veteran, brought his business expertise to the company.<sup>1</sup> Together, they set out to bring a new class of medications to transform the therapeutic area.

The initial phases of research for a new trabecular outflow drug were filled with twists and turns. As said by Dr. Kopczynski, "Innovation is rarely a linear process, especially in drug development. In a start-up, you have to be focused, but more importantly you have to follow the data, even if it takes you in a different direction than originally planned."<sup>1</sup> That is exactly what the dynamic and adaptable Aerie team did. Aerie began by pursuing ethacrynic acid and ticrynafen, compounds that Dr. Epstein's lab had studied for years. This proved to be a learning experience and led Aerie's chemists to generate related compounds. They continued investigating beyond their original territory of exploration—and an opportunity soon came in a drug discovery program focused on Rho kinase (ROCK) inhibitors.

The proposed mechanism of action and the promising therapeutic potential of ROCK inhibitors make for a highly anticipated glaucoma treatment option.<sup>3</sup> Although not entirely understood, it is believed that ROCK inhibitors bind to the protein Rho kinase. This seems to disrupt the binding interaction of myosin to actin and causes the stress fibers and anchoring complexes to disassemble. By reducing myosin-driven contraction in the TM, ROCK inhibitors appear to relax the meshwork. This facilitates increased outflow of nutritive aqueous humor through the tissue and reduces pressure in the eye.<sup>4</sup>

Our drug discovery program ultimately led us to the development of a new class of glaucoma therapeutics called ROCK inhibitors.<sup>1</sup> The first TM outflow drug in the pipeline, netarsudil ophthalmic solution 0.02%, has been shown in clinical studies to lower intraocular pressure (IOP).<sup>5</sup> Excitement is brewing as Aerie enters launch mode. “Due to the progressive nature of glaucoma, new therapies are needed that directly target the diseased TM to block or reverse its deterioration, and we believe netarsudil ophthalmic solution 0.02% has excellent potential to address this unmet need,” said Dr. Kopczynski. If approved, netarsudil ophthalmic solution 0.02% would become the only once-daily product available that specifically targets the TM.<sup>5</sup> Aerie isn’t stopping there. Aerie will be conducting additional clinical studies to characterize the performance of netarsudil ophthalmic solution 0.02%. The company is also taking the potential of netarsudil ophthalmic solution 0.02% a step further by undergoing Phase 3 trials for netarsudil 0.02%/latanoprost 0.005% ophthalmic solution, a fixed-combination formulation of netarsudil ophthalmic solution 0.02% and latanoprost, a PGA that is the most widely prescribed glaucoma drug in the US.<sup>6</sup>

“Being able to intervene early with a compound that targets the diseased tissue of the trabecular meshwork (TM), the main outflow drain in the eye is a critical unmet need,” said Dr. Kopczynski, Co-founder and Chief Scientific Officer. It was the quest for a trabecular outflow drug that led to the founding of Aerie Pharmaceuticals, Inc.

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