

BUILDING A MAJOR OPHTHALMIC PHARMACEUTICAL COMPANY

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.¹

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



Aerie Pharmaceuticals is a clinical-stage pharmaceutical company focused on the discovery, development, and commercialization of first-in-class therapies for the treatment of glaucoma and other diseases of the eye.

THE START OF AERIE: A COMPANY FOCUSED ON OPHTHALMOLOGY

Aerie began in 2005 after David Epstein, MD; Erik Toone, PhD; and Casey C. Kopczynski, PhD joined forces.¹ 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.² Dr. Kopczynski, a biotech start-up veteran, brought his business expertise to the company.¹ Together, they set out to bring a new class of medications to transform the therapeutic area.

"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.

MEET THE VISIONaerieS™



Vicente Anido, Jr, PhD

Chief Executive Officer and Chairman of the Board

Vicente Anido, Jr, PhD, has served as Chief Executive Officer since July 2013 and as Chairman of the Board since April 2013. Dr. Anido is the former President, Chief Executive Officer, and Director of ISTA Pharmaceuticals, Inc. Prior to joining ISTA Pharmaceuticals, Dr. Anido served as President of the Americas Region of Allergan, Inc., where he was responsible for Allergan's commercial operations for North and South America.



Casey Kopczynski, PhD

Chief Scientific Officer

Casey C. Kopczynski, PhD has served as Chief Scientific Officer and co-founder of Aerie since 2005. Before joining, he was the Managing Partner at Biotech Initiative, LLC, a consulting practice dedicated to emerging biotech companies. He was also previously the Vice President of Research at Ercole Biotech, Inc., where he was devoted to developing novel drugs for the treatment of cancer, inflammation, and orphan genetic diseases and to bringing advanced treatments to patients in need. Dr. Kopczynski received his PhD in molecular, cellular, and developmental biology from Indiana University and was a Jane Coffin Childs Research Fellow at the University of California, Berkeley. With more than 18 years of clinical experience, he has published over 40 research publications advancing scientific discovery.



Thomas Mitro

President and Chief Operating Officer

Thomas A. Mitro has served as President and Chief Operating Officer since August 2013. Previously, Mr. Mitro served as Vice President, Sales and Marketing at the clinical-stage biopharmaceutical company Omeros Corporation. Prior to this, Mr. Mitro was Vice President, Sales and Marketing at ISTA Pharmaceuticals for 10 years, where he was instrumental in building ISTA's commercial operations and launching several eye-care products.



Richard Lewis, MD

Chief Medical Officer

"It has been 20 years since glaucoma doctors have had a new medication in battling this disease," said Dr. Rick Lewis, Chief Medical Officer and past president of the American Glaucoma Society and ASCRS. "The glaucoma community has been looking for a new medication that enhances conventional outflow and is safe for patients, to complement existing medications in lowering IOP. I am excited about the opportunity to see this happen."



Theresa Heah, MD, MBA | Beth Shultz Scott, OD, MS Pharm | Kristine Erickson, OD, PhD

Clinical and Medical Affairs Team

The qualified clinical and medical affairs team is built on scientific and strategic acumen. Dr. Heah has extensive experience in the development of pharmaceutical technologies for retinal diseases and glaucoma. Dr. Schultz Scott's expertise in eye care spans clinical practice, academia, and industry. Dr. Erickson has deep academic ophthalmology experience and has been a key contributor to several clinical development programs. "I am excited to work with such an experienced and committed group to guide clinical research activities related to netarsudil and other first-in-class therapies," said Dr. Heah.



Judith Robertson | Michael Rowe | Evan Hockman | Mike McCleerey

Commercial Team

"I am excited to help bring the first truly new pharmaceutical option to the glaucoma market in more than 20 years," said Judy Robertson, Chief Commercial Officer. "Along with my experienced team—Mike, Michael, and Evan—all recognized within the glaucoma community, we are focused on sharing our vision of the future of glaucoma treatment."

THE SEARCH FOR A NEW TRABECULAR OUTFLOW DRUG

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." 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.¹

The contributions made by David Epstein and other glaucoma researchers to understanding the critical function of the trabecular outflow pathway in healthy and diseased eyes cannot be overstated. This work provided the foundation, as well as the inspiration, for Aerie's drug discovery efforts.

- Dr. Kopczynski, Co-founder and Chief Scientific Officer

UNLOCKING TRABECULAR OUTFLOW POTENTIAL WITH ROCK INHIBITORS

The proposed mechanism of action and the promising therapeutic potential of ROCK inhibitors make for a highly anticipated glaucoma treatment option3

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.⁴

FROM DISCOVERY TO DEVELOPMENT

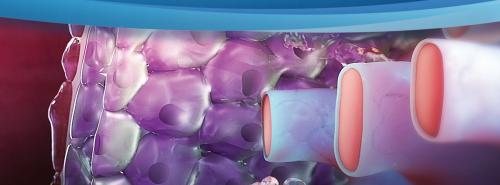
Our drug discovery program ultimately led us to the development of a new class of glaucoma therapeutics called ROCK inhibitors. The first TM outflow drug in the pipeline, netarsudil ophthalmic solution 0.02%, has been shown in clinical studies to lower intraocular pressure (IOP).

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.⁵

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.⁶

| Lead Product Candidates ⁷ | Proposed Pathway ^{5,6} | Phase of Development ⁷ | Intellectual Property Rights ⁷ |
|---|------------------------------------|-----------------------------------|---|
| Netarsudil ophthalmic solution 0.02% | TM outflow | NDA filed | Wholly Owned |
| Netarsudil 0.02%/latanoprost 0.005% fixed-combination ophthalmic solution | TM outflow/ uveoscleral outflow | Phase 3 | Wholly Owned |

 ROCK inhibitors appear to relax the TM, facilitating increased outflow of nutritive aqueous humor through the tissue⁴



We have such promise, with a combination of products in late stage development as well as early stage research. I believe that Aerie will be known 5 years from now as the leading ophthalmic pharmaceutical company.

- Rich Rubino, Chief Financial Officer



THE VISIONaerieS™ ARE CREATING A BRIGHTER FUTURE IN OPHTHALMIC CARE

Innovation and discovery at Aerie are a continuous journey that seeks to advance the knowledge of glaucoma and how to treat it. The company is currently investigating the disease-modifying potential of netarsudil ophthalmic solution 0.02% and other ROCK inhibitors. Recent preclinical studies have also shown that ROCK inhibitors may have an anti-fibrotic effect on the TM and the potential to increase perfusion of the TM.8

Aerie is also continuing exploration of drug delivery alternatives for their small molecules, including devices to optimize the duration of effect against diseases that affect the back of the eye. Drug devices are in development to treat age-related macular degeneration (AMD) and diabetic retinopathy and diabetic macular edema (DR/DME). These devices would address multiple drivers of disease including fibrosis, inflammation, vessel leakage, and neovascularization. Preclinical research has demonstrated efficacy as monotherapy and as an adjunctive to anti-VEGF therapy. The introduction of these devices has the potential to improve long-term outcomes.

I'm excited about discovery. It's all about learning something new and translating that new learning into an actual treatment that benefits patients. Anything we can do to further advance our knowledge and treatment of the disease—having the opportunity and tools to actually test these ideas in the clinic—and hopefully be successful ultimately in bringing a new treatment to patients...it's incredibly exciting. It's motivating for me and everyone at Aerie.

- Dr. Kopczynski, Co-founder and Chief Scientific Officer

With a proprietary library of more than 4100 investigational compounds, the potential for innovation is endless. The beneficial effect of ROCK inhibitors on the underlying disease processes of inflammation, fibrosis, and angiogenesis may have the potential to provide new mechanisms and pathways to treat AMD and other sight-threatening diseases.¹⁰

Aerie is well on its way to becoming a fully integrated commercial ophthalmic company with products to treat beyond just glaucoma, but retinal diseases as well.

References

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