# Novel regenerative peptide therapy for dry eye disease, BRM421, advances to Phase 3 clinical trials

BRIM Biotechnology, Inc. has advanced its lead candidate for dry eye disease (DED), BRM421, to Phase 3 clinical trials, following the submission of the clinical trial protocol to the US Food and Drug Administration (FDA) in December 2022.

BRM421 is a novel, first-in-class regenerative peptide therapy for moderate-to-severe DED treatment with a multi-modal mechanism of action. BRM421 speeds up the cornea repair process through stimulation of corneal stem cell proliferation and differentiation, anti-inflammation and meibomian gland recovery.

The Phase 3 clinical trial for BRM421 is a multi-centre, double-blind, randomised, placebo-controlled trial in the United States. Enrolment is currently underway for more than 700 patients with moderate to severe DED. The clinical trial is expected to be completed in Q4 2023.

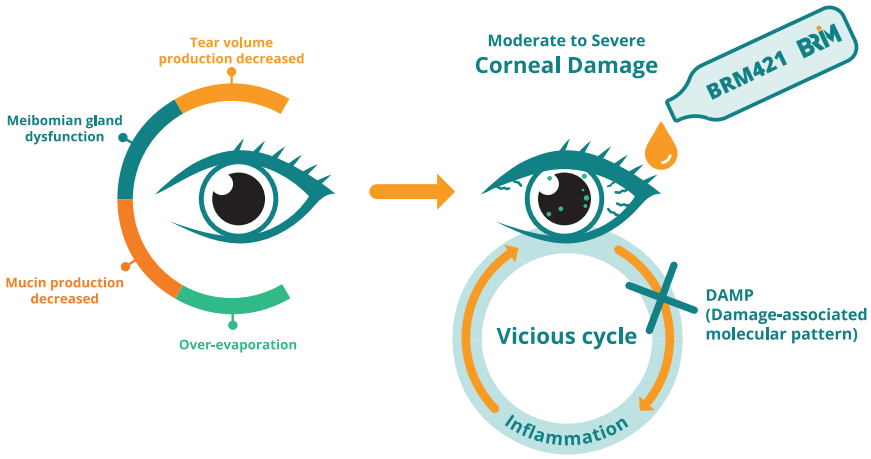


Figure 1: Through its multi-modal mechanism of action, BRM421 has the potential to break the vicious cycle of corneal damage in dry eye disease, offering patients rapid and total relief.

**BRM421: Breaking the vicious cycle of DED**

"There is currently no cure for DED, and there is a lack of treatment options available to patients. Currently, more than half of prescription drugs are anti-inflammatory medicines, and the rest are artificial tears or lubricants. These types of treatments are often not enough to control discomfort for moderate to severe patients unless there is a way to further speed up the healing process. Due to its unique mechanism of action, BRM421 has the potential to become the first DED treatment to offer rapid and total relief," said Dr. Haishan Jang, Chair and CEO of BRIM.

Patients and clinicians urgently need more effective therapies. DED results from various defects affecting proper tear production and the composition of the tear film. These include decreases in both tear volume and mucin production, and dysfunction of the meibomian glands. Without normal tear lubrication of the corneal surface, corneal damage can occur, leading to non-infectious inflammation and further damage to the corneal surface via lymphocyte infiltration and proinflammatory cytokines. This vicious cycle worsens DED and impairs a patient's quality of life.

**Unique multi-modal mechanism of action**

BRM421 has the potential to break the vicious cycle of corneal damage by stimulating the body's own cells to repair and regenerate at the site of damage. The active pharmaceutical ingredient of BRM421 is a synthetic peptide composed of 29 amino acids derived from a multifunctional protein, pigment epithelium-derived factor (PEDF), with neurotrophic and anti-inflammatory properties. The functional domain of PEDF chosen to generate PEDF-derived short peptides (PDSP) also has a unique mechanism of action that promotes the "stemness" of certain types of cells, including mesenchymal stem cells.

Mesenchymal stem cells can differentiate into multiple tissue types, including bone, cartilage, muscle and fat cells and connective tissue. Therefore, BRIM's PDSPs have the potential to treat other conditions, such as osteoarthritis, by promoting cartilage regeneration, repairing damage, and relieving joint pain.

BRM421 has shown promising clinical outcomes in two Phase 2 studies; treatment with BRM421 ophthalmic solution significantly improved DED symptoms including dryness, burning, stinging and photophobia within one week of treatment. Most patients reported they felt less burning and stinging in the morning and less dryness in the evening – times when DED sufferers usually feel most uncomfortable. In addition, BRM421 also showed efficacy in repairing the cornea in 15 days. The data showed that BRM421 has an early onset of action and is well tolerated.

**The power of regenerative peptides**

Novel regenerative peptides such as BRM421 offer a new and exciting type of treatment with several advantages over other therapies. Compared to full-size proteins, peptides penetrate tissues more effectively to reach local stem cells, especially for topical applications. Peptides also limit systemic exposure, which reduces unwanted side effects.

Additionally, because short peptides can usually be synthesised chemically, manufacturing costs are likely to be much lower than for therapies that rely on growth factors or stem cells. With better long-acting and slow-release formulation technologies, regenerative peptides have the potential to become an ideal new class of therapies in DED treatment.

The advancement of BRM421 to Phase 3 clinical trials brings BRIM one step closer to achieving its vision of providing the millions of people around the world living with DED with an effective and affordable treatment option.