

Development of BTX-001, a novel AAV-Mediated Intravitreal Gene Therapy Delivering a C5 Inhibitor for Geographic Atrophy

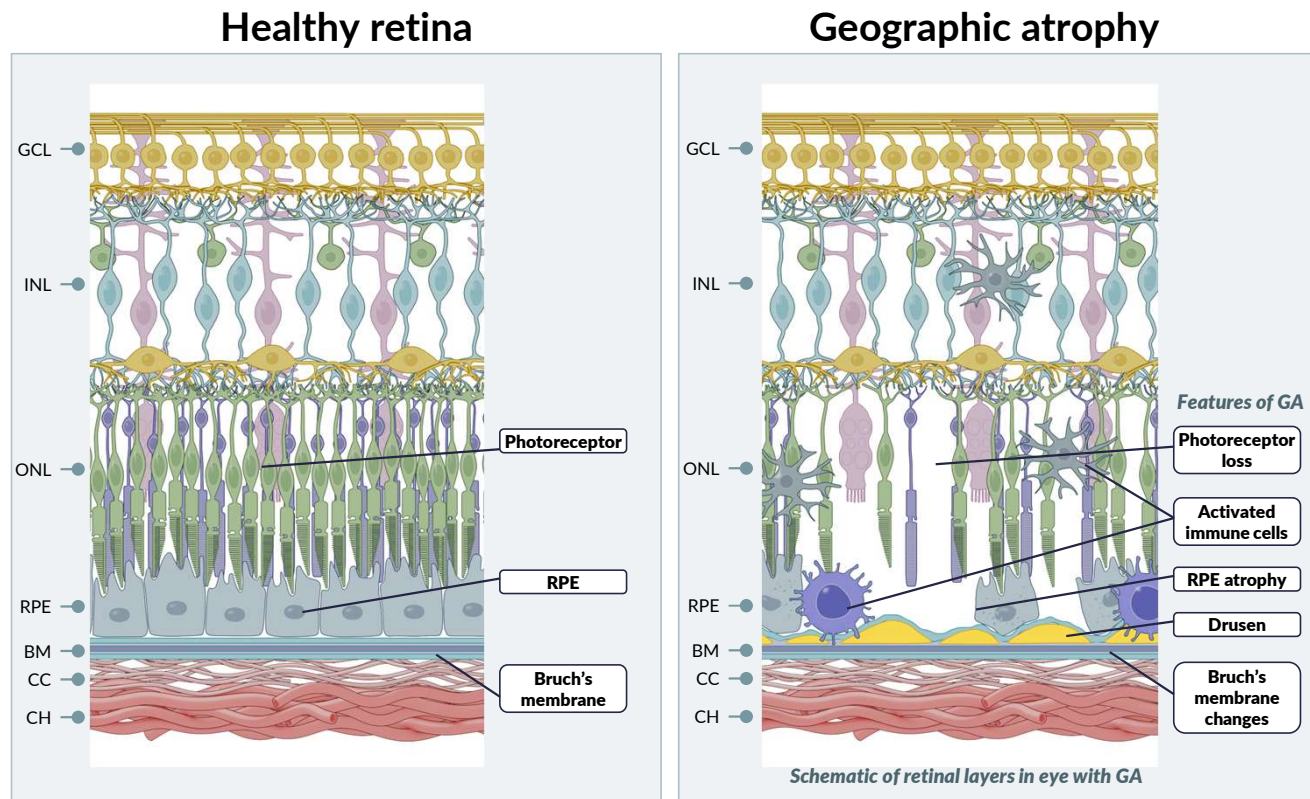
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BTX-001 is an investigational product; it has not been approved by the FDA. Conclusive evidence of efficacy and safety of BTX-001 will require further investigation in clinical trials. Beacon Therapeutics, Inc. was the sponsor of this presentation.

Geographic Atrophy Drives Progressive, Irreversible Vision Loss



GA is a leading cause of vision loss in older adults

Characterized by **progressive and irreversible loss** of photoreceptors, retinal pigment epithelium, and underlying choriocapillaris^{1,2}

1. Fleckenstein M et al. *Ophthalmology*. 2018; 125(3):369-390. 2. Fleckenstein M et al. *Nat Rev Dis Primers*. 2021;7(1):31.

BM, Bruch's membrane; CC, choriocapillaris; CH, choroid; GA, geographic atrophy; GCL, ganglion cell layer; INL, inner nuclear layer; MAC, membrane attack complex; ONL, outer nuclear layer; RPE, retinal pigment epithelium

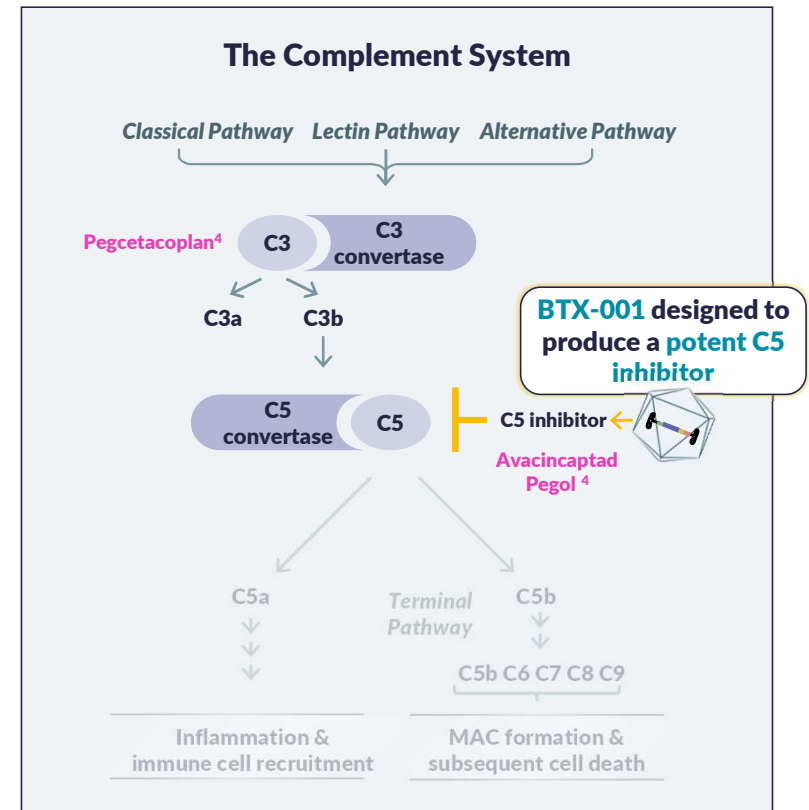
Complement is a clinically validated target in Geographic Atrophy

Genetic evidence: GWAS studies implicated complement dysregulation as a key player in disease pathology¹

Biological validation: Elevated complement activation products found in eyes and blood of AMD patients^{2,3}

Clinical validation: 2 approved complement therapies for GA. Both require frequent injections

BTX-001 is an investigational, one-time intravitreal gene therapy targeting the clinically validated, FDA approved, target C5



¹ Fritsche, LG et al. *Nature genetics*. 2016; 48(2):134-143. ² Mullins RF et al. *Eye*. 2001, 15:390-395. ³ Heesterbeek TJ et al. *Invest Ophthalmol Vis Sci*. 2020 Mar 16;61(3):18. ⁴ FDA approved IVT therapy AMD, Age-related macula degeneration; GA, Geographic atrophy; GWAS, Genomic wide association studies

Rational Design of BTX-001 for Durable Intravitreal Gene Therapy

Potent C5 Inhibitor

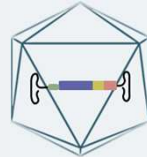


Small, secreted protein

High potency

Cell-type independent activity

Optimized Expression Cassette

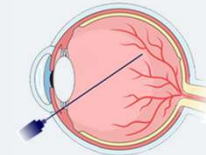


Strong, sustained expression

Efficient vector packaging

High full:empty ratio

IVT-Optimized Capsid



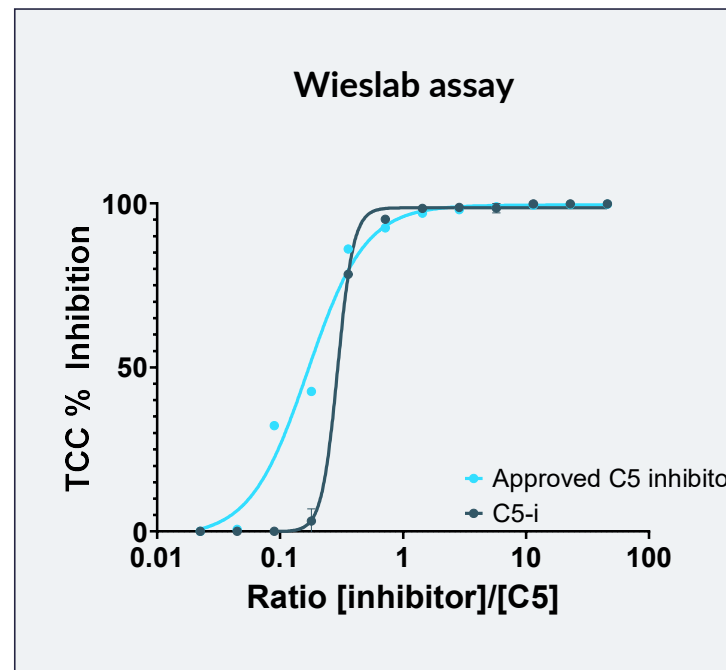
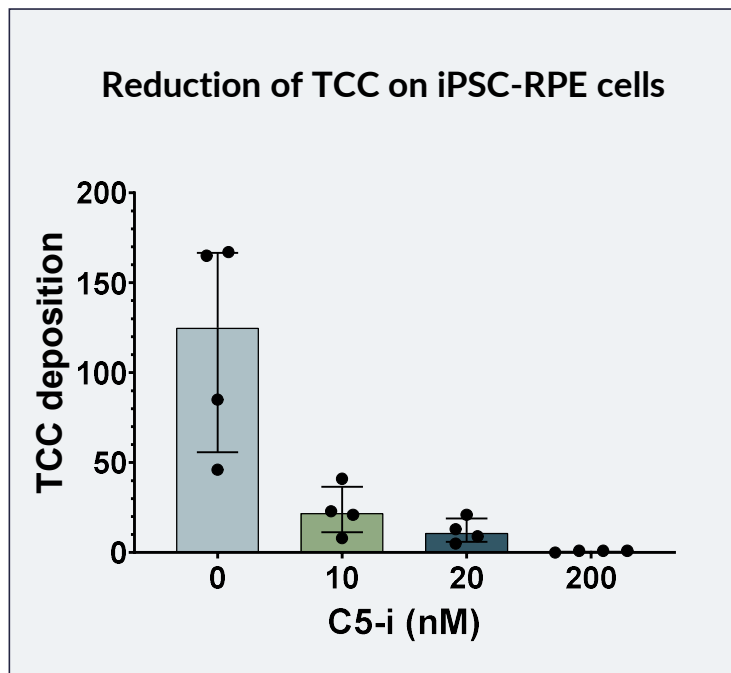
Efficient retinal transduction

Broad distribution

Favorable inflammatory profile

Designed to enable durable C5 inhibition with low treatment burden

BTX-001 Enables Potent and Specific In Vitro Inhibition of C5



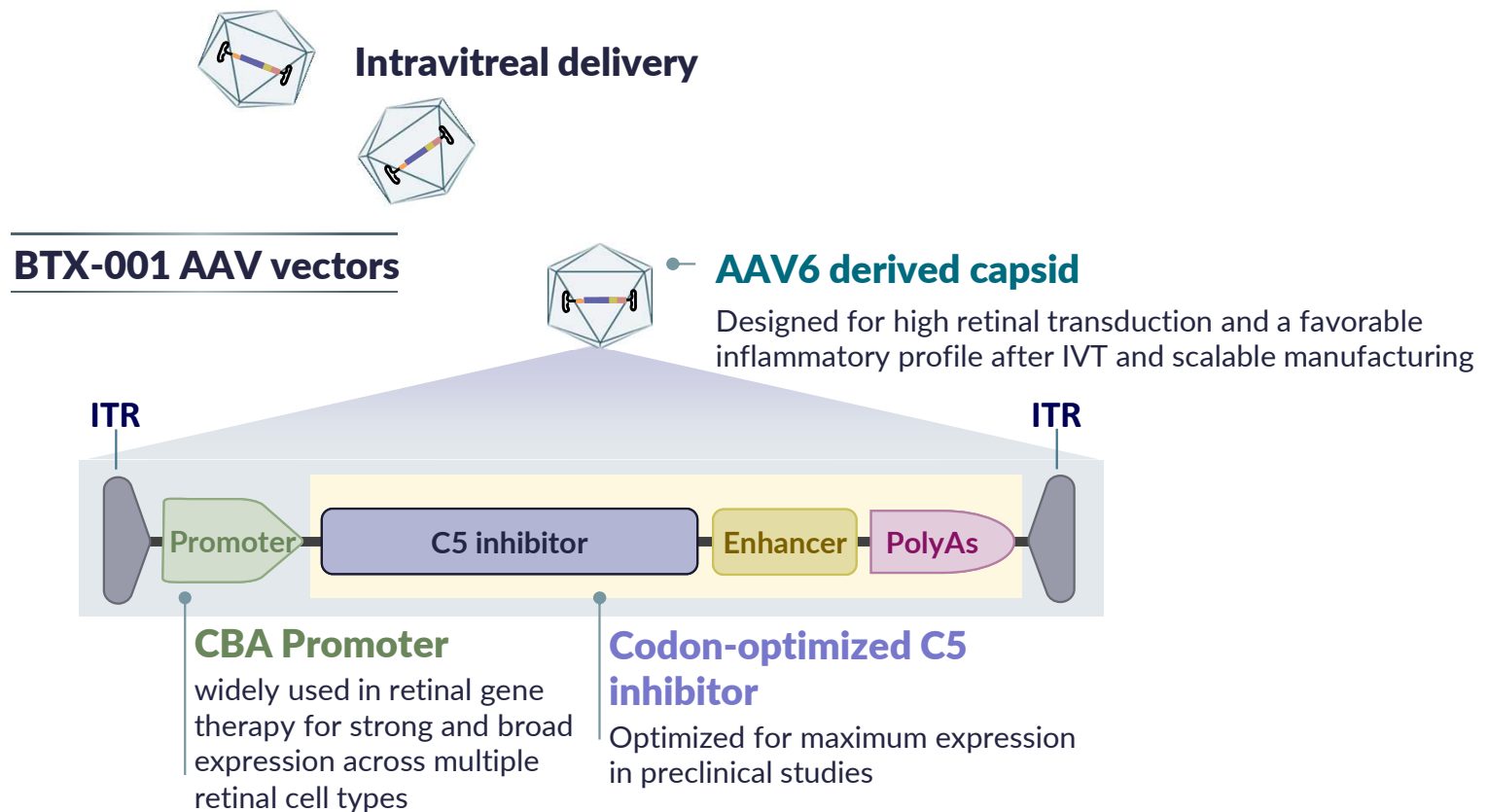
C5 Specificity confirmed
Target engagement and biological activity confirmed

Determined amount of C5-i required for inhibition of 99% of C5 in the human eye ^{1,2}

Translation from in vitro potency to human therapeutic levels

¹ Hallam TM et al. *eLife*. 2025;13:RP99806
iPSC-RPE, induced pluripotent stem cells; RPE, retinal pigment epithelium; TCC, Terminal complement complex

BTX-001 Encodes a Secreted, Potent C5 Inhibitor Optimized for Ocular Expression



In Vivo Studies Support Expression, Safety, and Translation

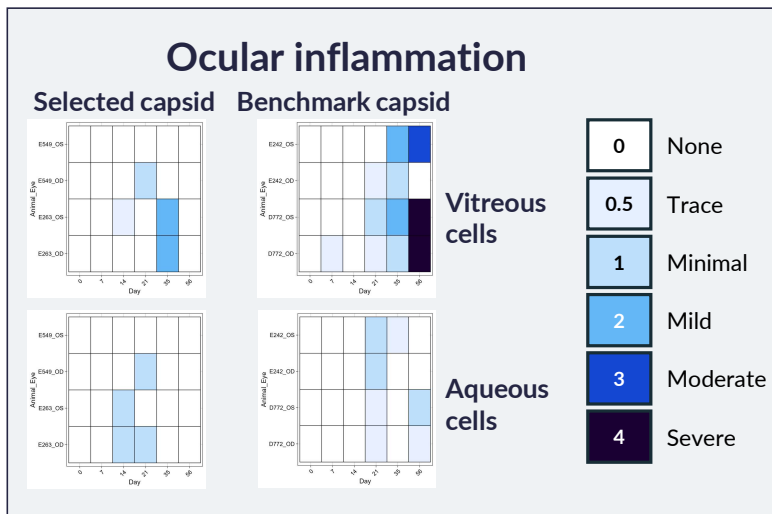


Study	Objective
Research studies in mice	Cassette optimization and expression
Research study in African Green Monkeys	Capsid selection
Research study in African Green Monkeys	Information for BTX-001 dose selection in GLP study, expression and ocular distribution
GLP compliant study in Cynomolgus Monkeys	Safety and biodistribution

Optimized Capsid Enables Efficient IVT Retinal Transduction in NHP

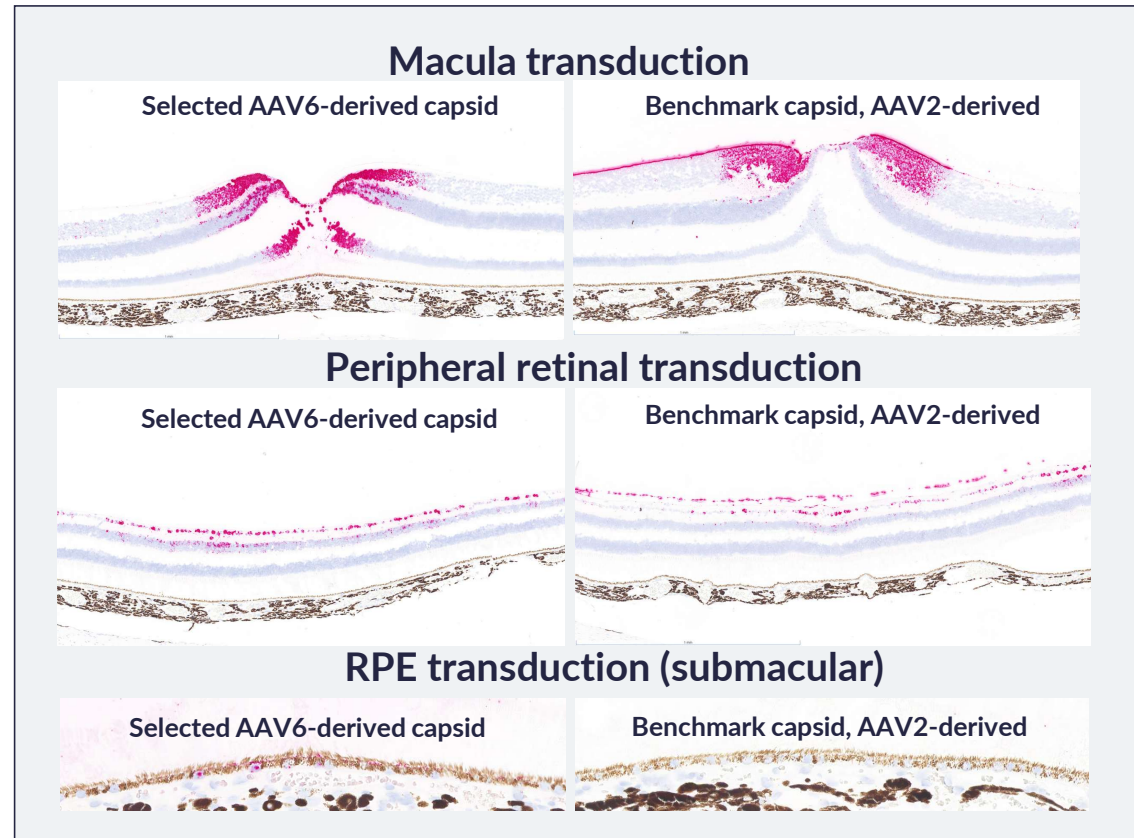


20 capsids screened → 10 advanced → 1 selected



Selected capsid shows:

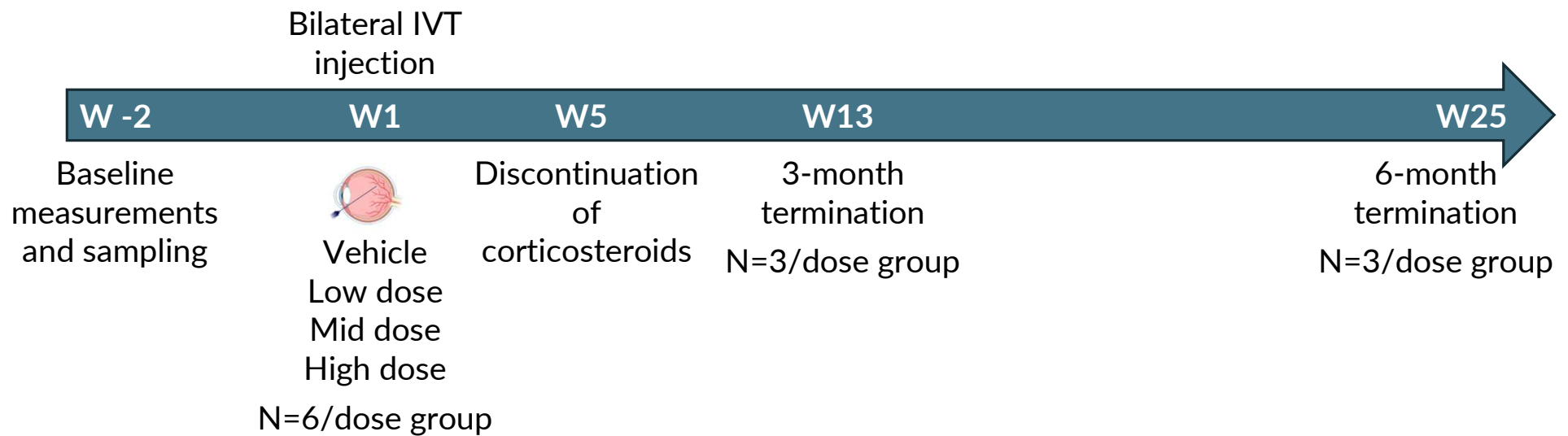
- ✓ Broad retinal transduction
- ✓ Favorable inflammatory profile



GLP Study Design Supports Comprehensive Safety Evaluation

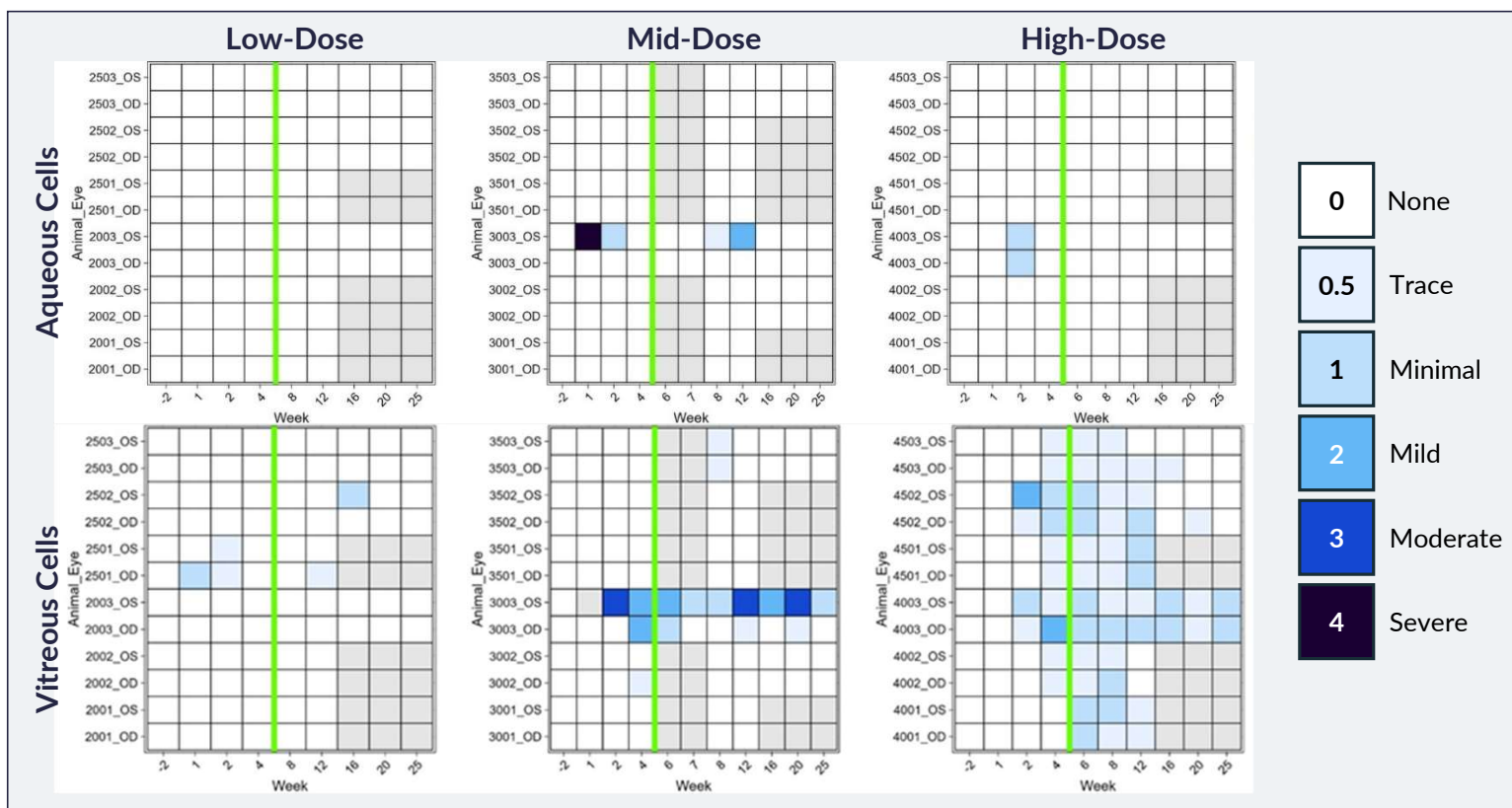


6-month GLP NHP study with multi-dose evaluation



Collection of serum, plasma, aqueous and vitreous humor, shedding matrices, ophthalmic examination, IOP, OCT, cSLO, ERG

BTX-001 Was Well Tolerated with Minimal Ocular Inflammation in NHP

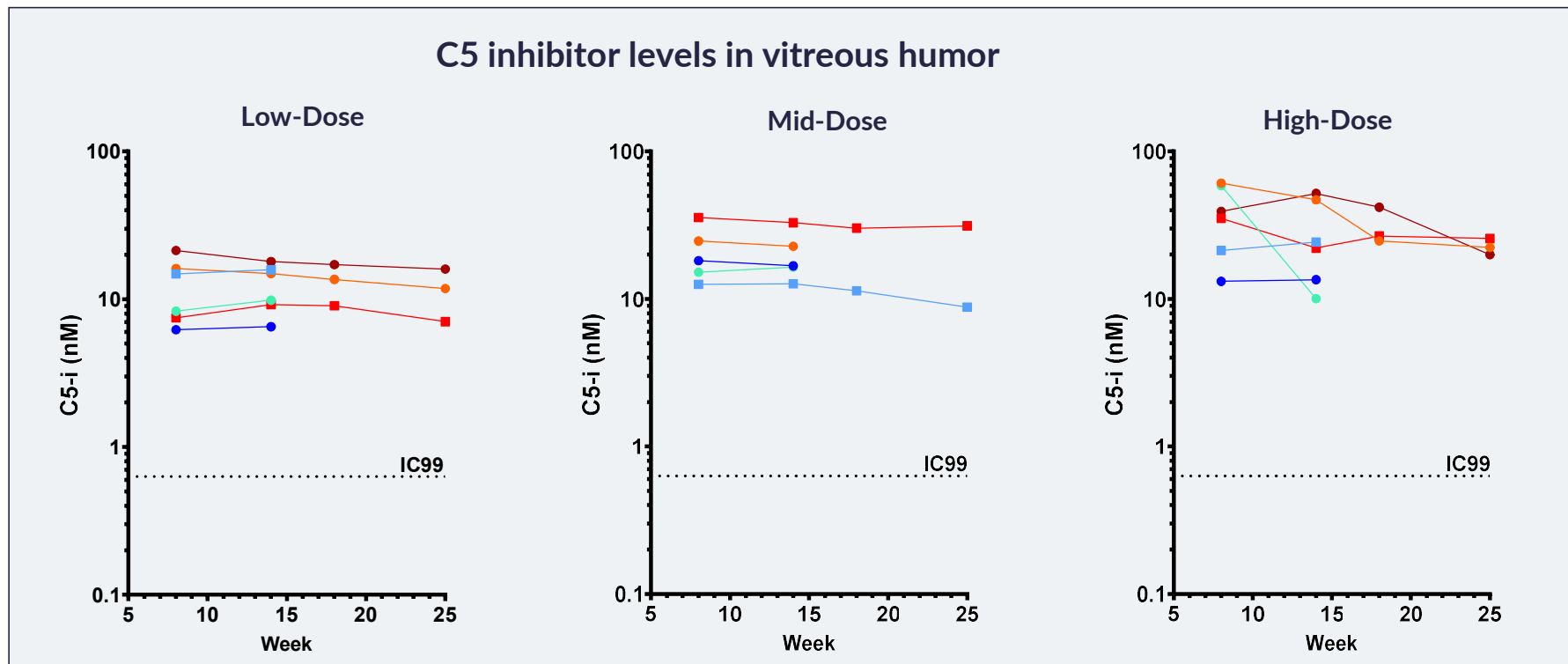


Ocular findings

- Well tolerated across doses
- Transient, dose-dependent inflammation
- No changes in IOP, OCT, or ERG

ERG, electroretinogram; IOP, intraocular pressure; OCT, optical coherence tomography
 Green line indicates the 5-week termination timepoint for IM immunosuppression (methylprednisolone); NHP, non-human primate

Sustained Expression Exceeded Levels Required for Complete C5 Inhibition in NHP



All doses achieved calculated therapeutic levels

BTX-001 Demonstrates a Strong Preclinical Profile

Potent C5 inhibition

Efficient IVT delivery

Favorable safety in NHP

Sustained therapeutic expression

Completed IND-enabling NHP studies

Advancing to clinical trials in 2H 2026

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Abraham Scaria



Learn more about BTX-001:

At the ASGCT Annual meeting,
Boston, MA – May 11-15, 2026
Poster # 2439
Wed, 13th May

And the rest of the Beacon team

<https://www.beaontx.com>