TWO PHASE 3 STUDIES OF THE SAFETY AND EFFICACY OF FIXED COMBINATION PHENYLEPHRINE 2.5%-TROPICAMIDE 1% OPHTHALMIC SOLUTION ADMINISTERED WITH A MICRODOSE DISPENSER FOR DILATION OF THE PUPIL (MIST-1 & MIST-2)

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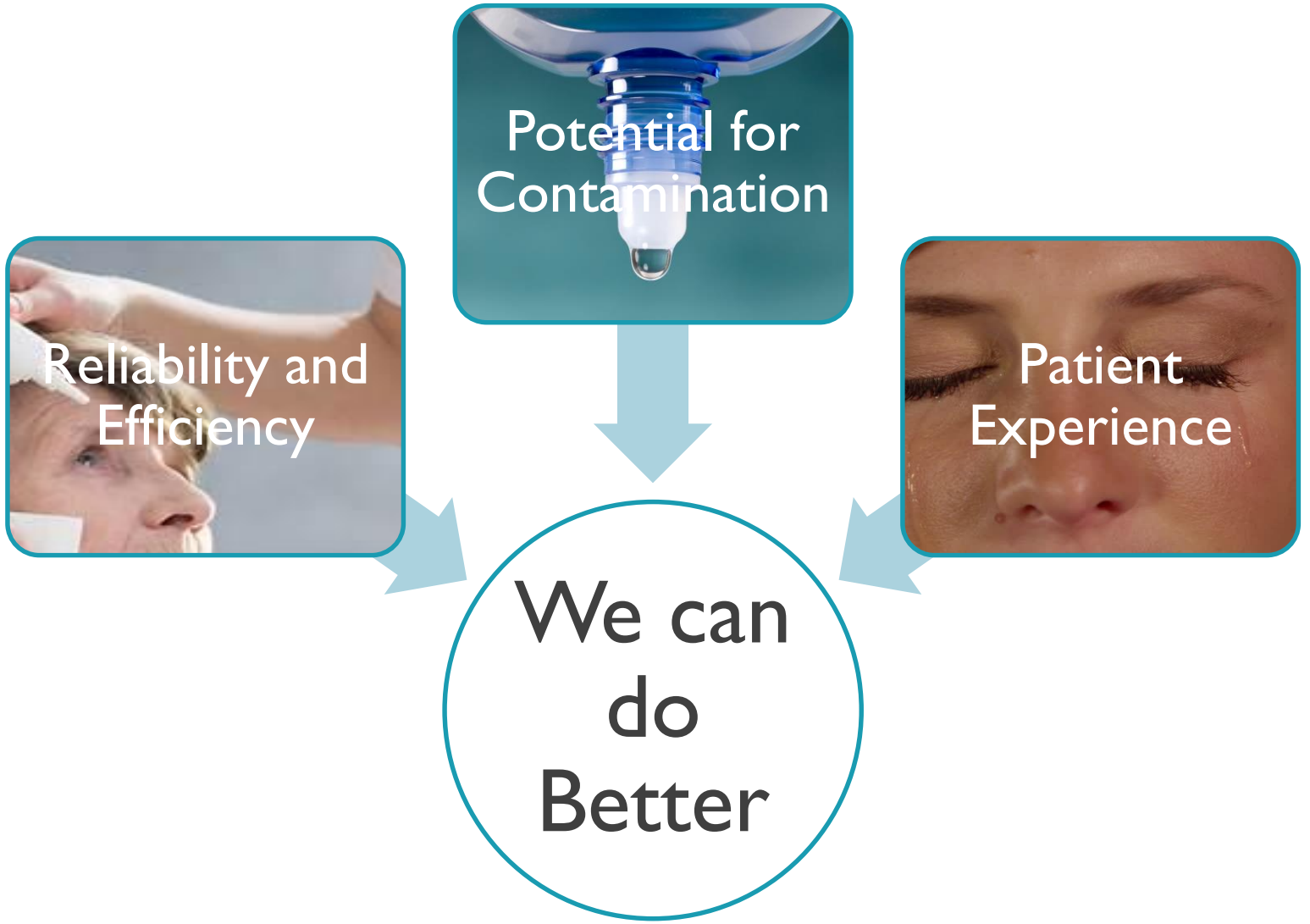
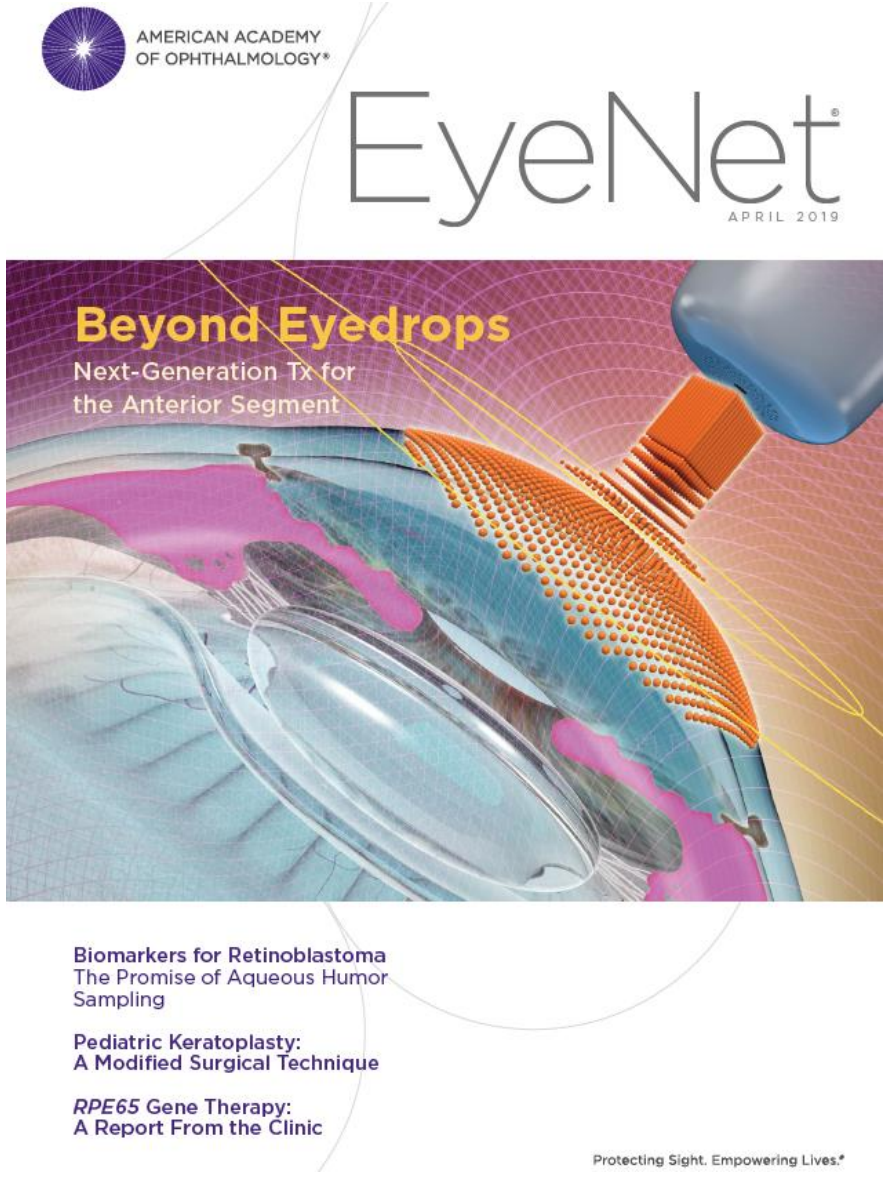
Disclosures

- Grant support from . . .
  - Alcon
  - Allergan
  - Annexon
  - Eyenovia (sponsor of the MIST-1 and MIST-2 study)
  - InSite
  - Kala
  - Nicos
  - Novartis
  - Ocugen
  - Ocular Therapeutix
  - Ora
  - Orasis
  - Santen

Pharmacological Mydriasis Today



Microdose Piezo-Print Technology



- Piezo-print technology[1]
  - Designed to Deliver ~ 8 µL of drug directly to the cornea
    - Standard eye drops are 35 µL
  - Consistent w/capacity of tear film; may avoid overdosing and overflow with its potential for systemic absorption
- Comparable efficacy of micro-dosing with traditional eyedropper dosing demonstrated with latanoprost[1]
- Potential for improved adverse event profile

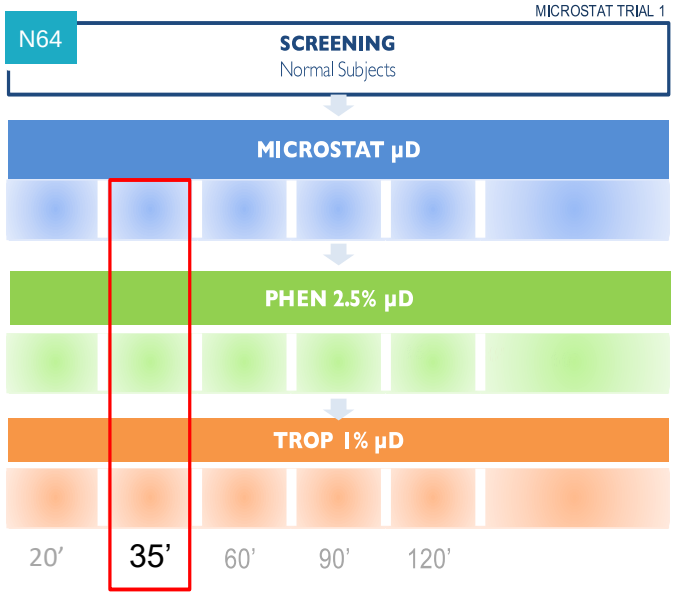
[1] Latanoprost with high precision, piezo-print microdose delivery for IOP lowering: clinical results of the PG21 Study of 0.4µL daily microdose. Pasquale LR, Lin S, Weinreb RN, Tsai JC, Kramm RL, Ianchulev T. Clinical Ophthalmology 2018

MicroStat Registration Program
Two Phase 3 Superiority Trials (MIST-1 & MIST-2)

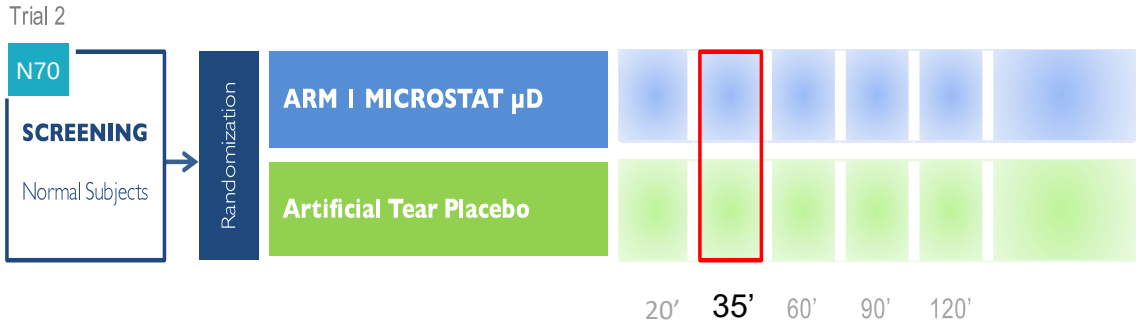
CLINICAL TRIAL DESIGN

- Double-masked, active-controlled, cross-over design
- MIST-1 (N 64 treated): µD phenylephrine-tropicamide vs µD tropicamide vs µD phenylephrine
- MIST-2 (N 70 treated): µD phenylephrine-tropicamide VS µD placebo

MIST-1



MIST-2



- **Primary EP: Mean change in pupil diameter at 35' vs BL**
- Hypothesis: MicroStat superior to Phen, Trop and placebo
- Power at 90% for each study
- All treatments administered using Optejet™ dispenser technology

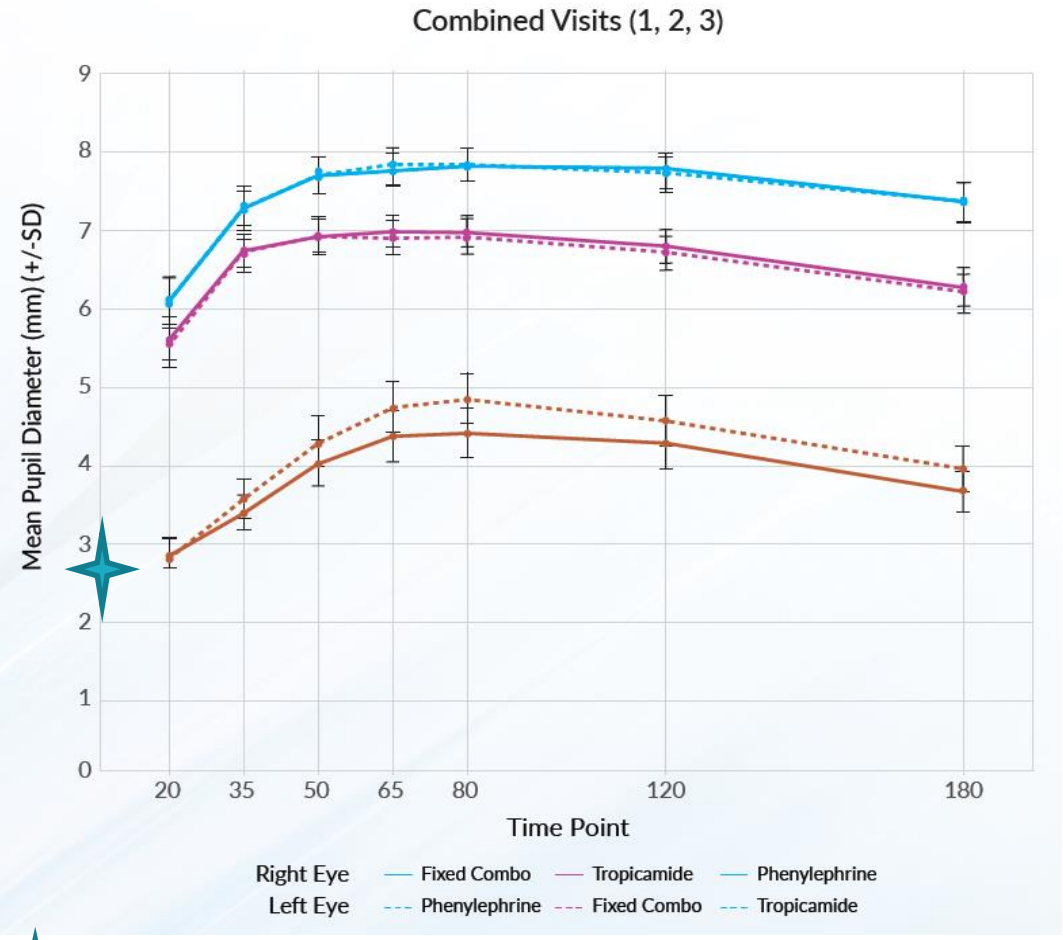
MIST-1/MIST-2
Study Demographics

	MIST-1 N = 64	MIST-2 N = 70
Age (years)		
Mean (SD)	39.4 (12.0)	35.4 (14.6)
Min, Max	12, 64	13, 66
< 17 years	1 (1.6%)	5 (7.1%)
Gender		
Male	37 (57.8%)	37 (52.9%)
Female	27 (42.2%)	33 (47.1%)
Ethnicity		
Hispanic/Latino	22 (34.4%)	35 (50.0%)
Race		
Asian	8 (12.5%)	1 (1.4%)
Black/African American	19 (29.7%)	7 (10.0%)
White	35 (54.7%)	62 (88.6%)
Multi-race	2 (3.1%)	-
Iris Color Category		
Light	10 (15.6%)	20 (28.6%)
Dark	54 (84.4%)	50 (71.4%)

- Similar demographics in both studies
- Study subject ages ranged from 12 – 66 years
- Prevalence of dark irises in study population

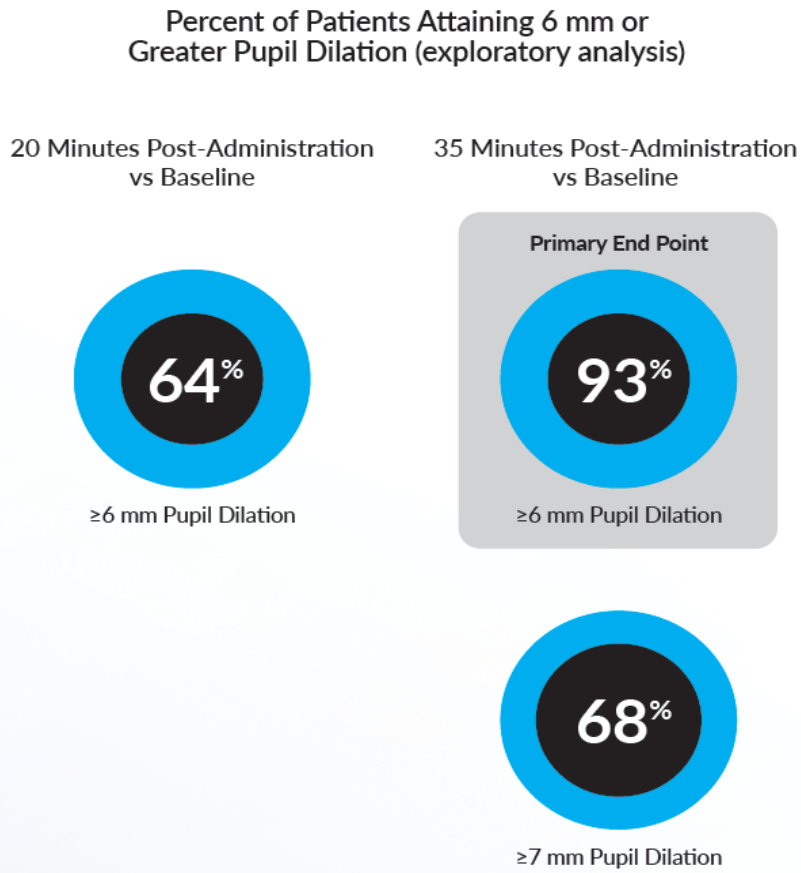
MIST-1/MIST-2 Efficacy

MIST-1



Baseline mean pupil diameter for all groups was 2.7 (OD) and 2.6 (OS)

MIST-2



MIST-1/MIST-2
Safety

- AEs reported were generally mild
- All were transient in nature.
- Consistent with types of AEs associated with mydriatic agents

	MIST-1*			MIST-2**	
	Fixed Combination phenylephrine 2.5% / tropicamide 1% (N = 62)	Tropicamide 1% (N = 64)	Phenylephrine 2.5% (N=62)	Fixed Combination phenylephrine 2.5% / tropicamide 1% (N = 69)	Placebo (N=70)
Adverse Events n (%)	2 (3%)	4 (6%)	3 (5%)	2 (3%)	0 (0%)

*AEs reported: mild blurred vision, mild eye pain, and mild transient reduction in visual acuity
**AEs reported: mild discomfort with drug administration and moderate photophobia

MIST-1 and MIST-2
Efficacy and Safety Conclusions

- In these two phase III studies, a fixed combination of micro-dosed phenylephrine 2.5% and tropicamide 1% ophthalmic solution was shown to be safe and effective for pharmacologic mydriasis
  - Approximately 94% of treated eyes achieved 6mm or greater dilation at 35 minutes post-instillation
  - Adverse events were infrequent (~ 3% of patients) and majority were mild

- An exploratory analysis shows that dilation is rapid in most patients
  - Up to 64% of fixed-combination treated eyes achieved 6mm or greater dilation at 20 minutes post-installation

MIST-1 and MIST-2 Usability Conclusions

- The design of the Optejet™ dispenser may minimize cross-contamination, enhance office efficiency and improve the patient experience
  - No protruding parts to touch the ocular surface
  - Micro-dosing allows less product to overflow the eye

- These outcomes further validate the ability to maintain efficacy and potentially improve on the therapeutic index by delivering topical ophthalmic medication with piezo-print micro-dosing technology