APP13007
(Clobetasol Propionate Ophthalmic Nanosuspension) for the Treatment of Inflammation and Pain after Cataract Surgery

Jeffrey Levenson, M.D. [1], Thomas R. Walters, M.D. [2], Joseph Martel, M.D. [3], Laurene Wang, Ph.D. [4], Derek Nunez, M.D. [4]

[1] Levenson Eye Associates, [2] Keystone Research, [3] Martel Eye Medical Group, [4] AimMax Therapeutics, Inc.

Objective and Background

AIM: To evaluate the safety and efficacy of APP13007 for the treatment of inflammation and pain after cataract surgery in a double-masked, placebo-controlled, 2-part (A and B) Phase 2 study.

- APP13007 is an opalescent liquid of a novel, aqueous ophthalmic nano-suspension of Clobetasol Propionate for convenient multi-dose dispensing.
- Clobetasol Propionate is the most potent corticosteroid used in clinical practice, but previously has only been available for topical dermal use.
- In nonclinical studies, APP13007 shows good penetration of Clobetasol Propionate into ocular tissues after instillation into the conjunctival sac.

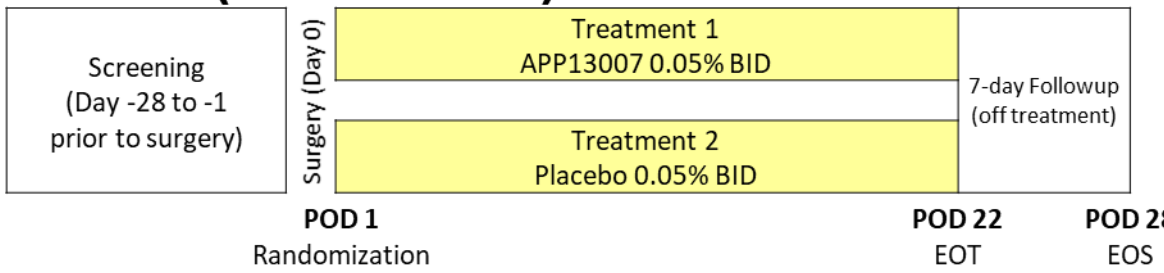
Study Design

Two-part Study (A and B)

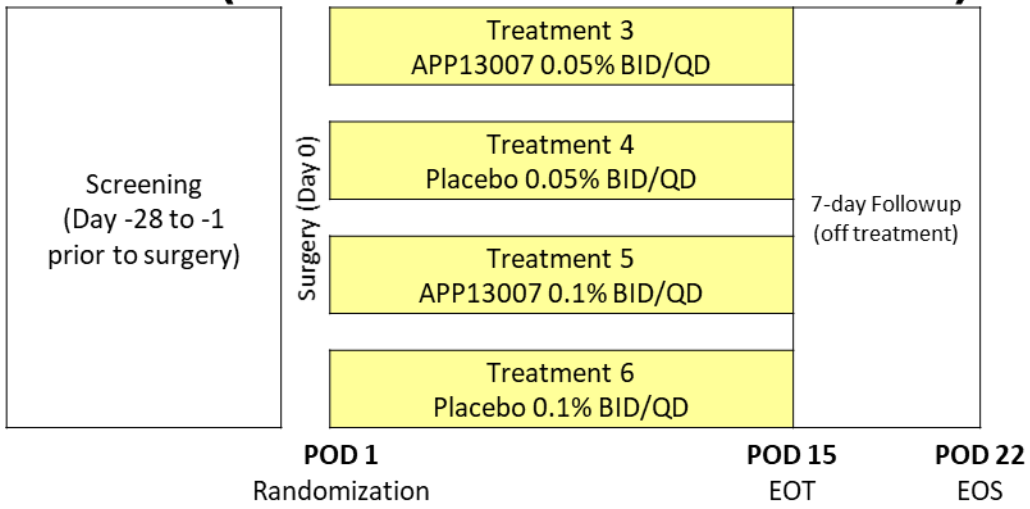
- Eligible subjects assessed and randomized 1 day after routine uncomplicated cataract surgery, i.e., on post-operative day (POD) 1 = baseline
- Further assessments
  - Part A: POD4, 8, 15, 22 and post-treatment POD28
  - Part B: POD4, 8, 15, and post-treatment POD22

- Two strengths (0.05% and 0.1%) and two dosing regimens:
  - Part A: 1 drop 0.05% APP13007 or Placebo BID for 21 days
  - Part B: 1 drop 0.05% or 0.1% APP13007 or matching Placebo BID for 3 days followed by 1 drop QD for 11 days

Part A (0.05% BID)



Part B (0.05% and 0.1% BID/QD)



Key Inclusion/Exclusion Criteria

- Age ≥ 50 years
- Males and Females (only females of non-childbearing potential)
- No medical and surgical conditions and prohibited medications that could confound study outcomes and/or subject safety or wellbeing

<u>Post-Op Day 1 (POD1)/Day of Randomization</u>

- Had unilateral uncomplicated cataract extraction and lens implantation
- Had > 10 cells and ≤ 30 cells in the anterior chamber
- Had an IOP ≤ 30 mmHg.

Disposition and Demographics

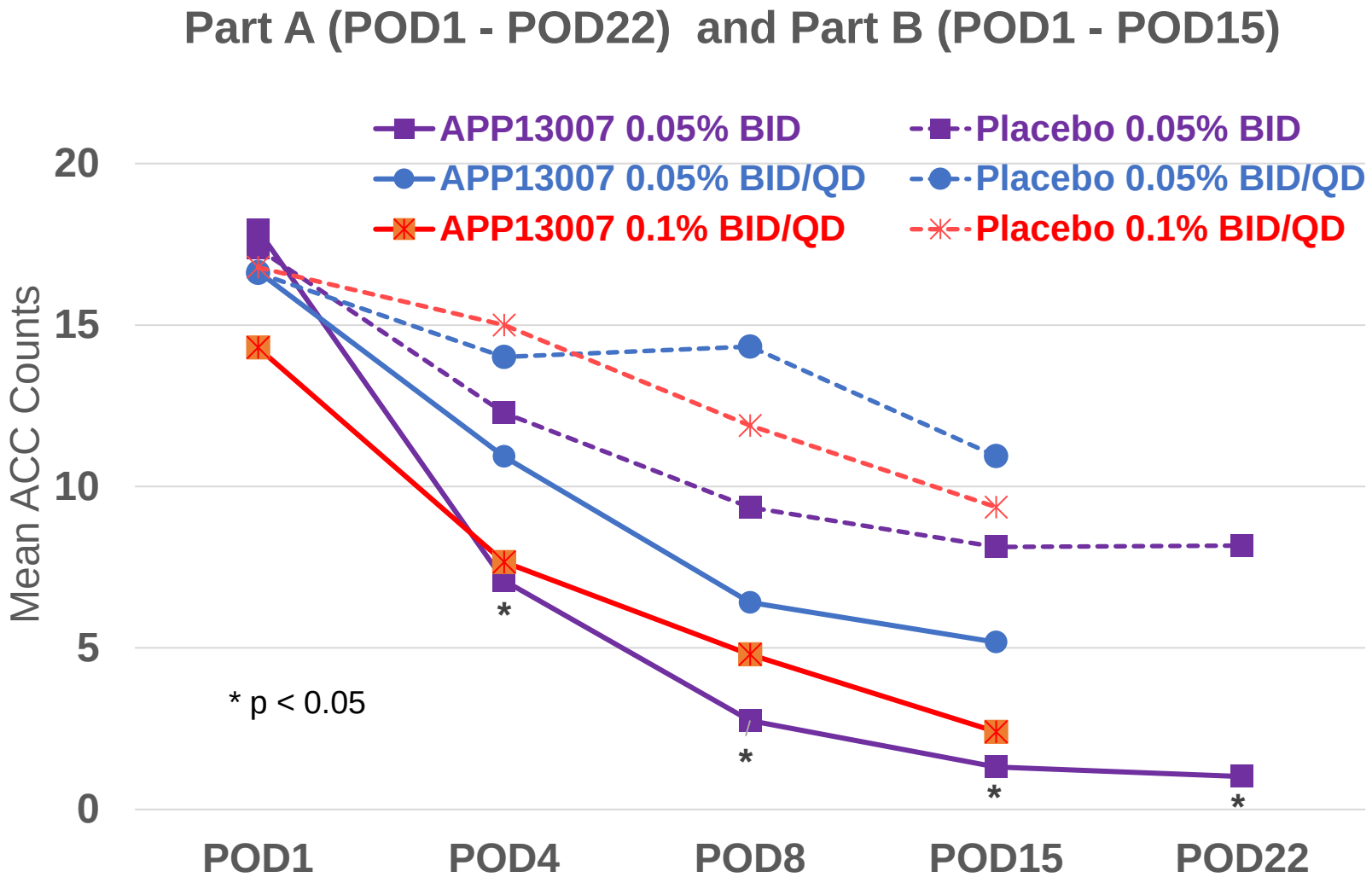
- Part A: 45 subjects randomized and received Study Drug
  - 7 subjects were rescued or withdrawn before POD22
- Part B: 87 subjects randomized and received Study Drug
  - 15 subjects were rescued or withdrawn before POD15

Typical of subjects who have Cataract Surgery in US:

- Mean Age: ~68 years
- Gender: Females > Males
- Race: White (incl. Hispanic) > Black > Asian

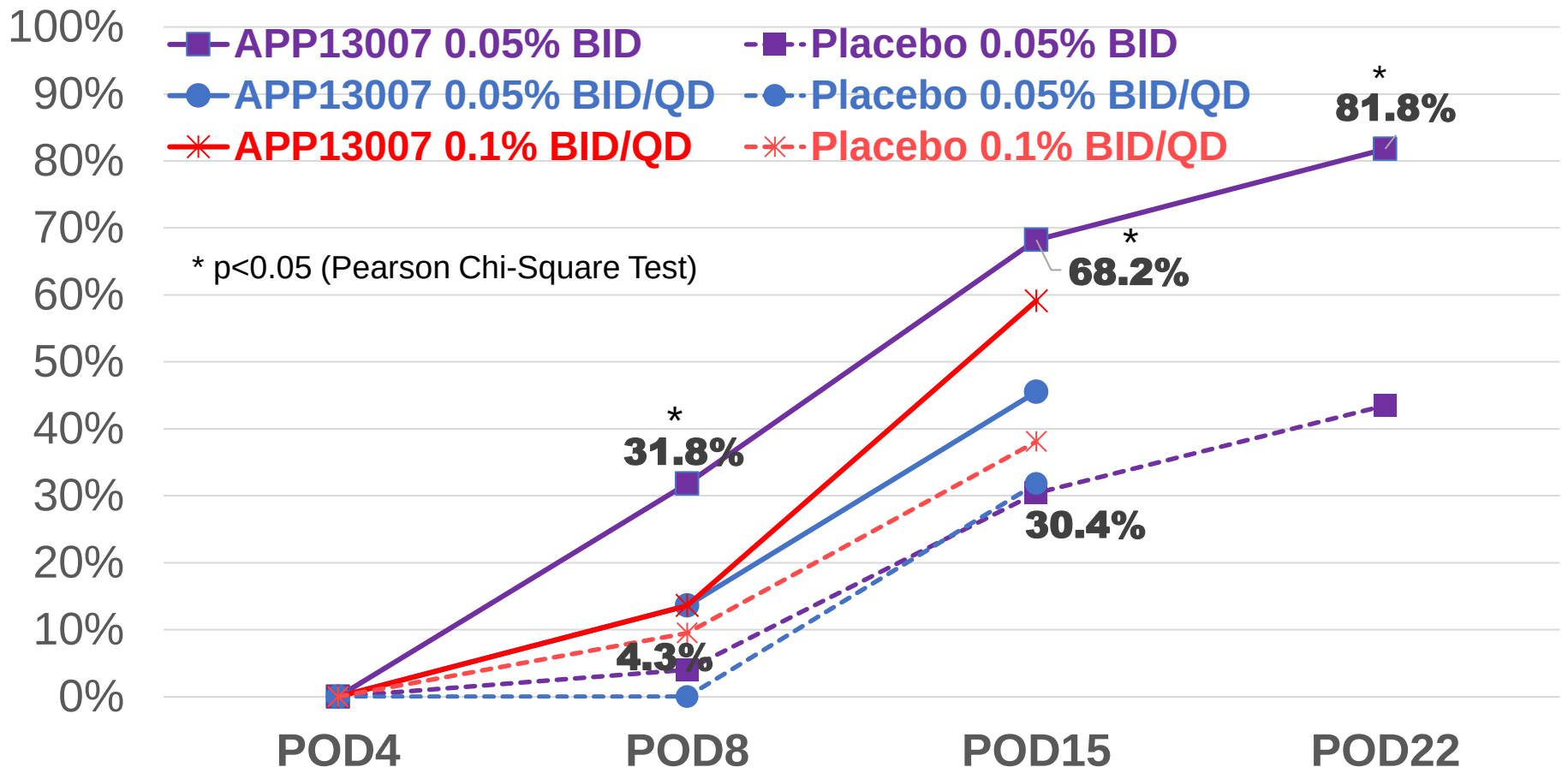
Baseline characteristics were comparable between the APP13007 and matching placebo groups

Mean Anterior Chamber Cell (ACC) Counts



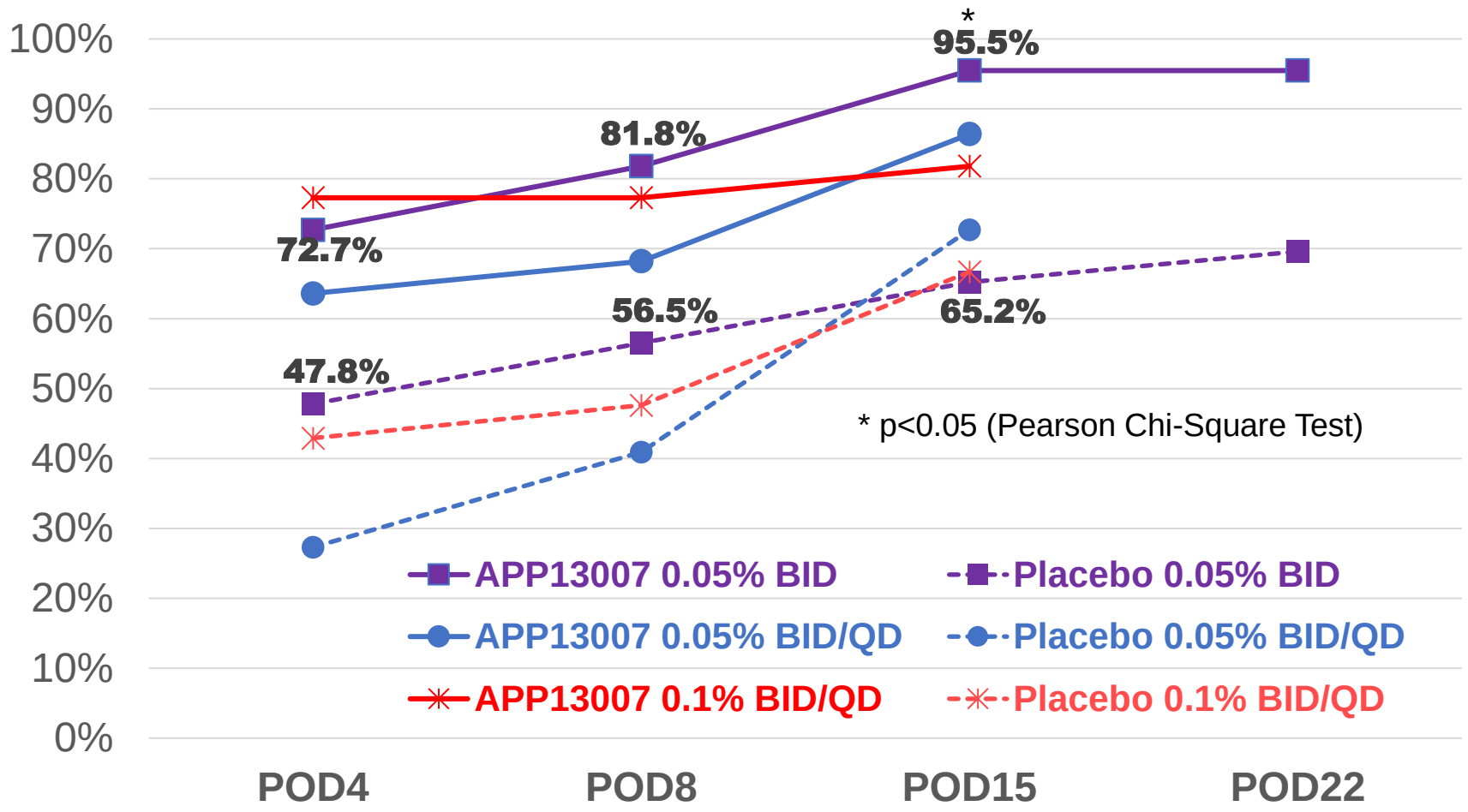
Sustained ACC Count=0/Grade = 0

(sustained from POD8 to POD22 in Part A or POD15 in Part B)



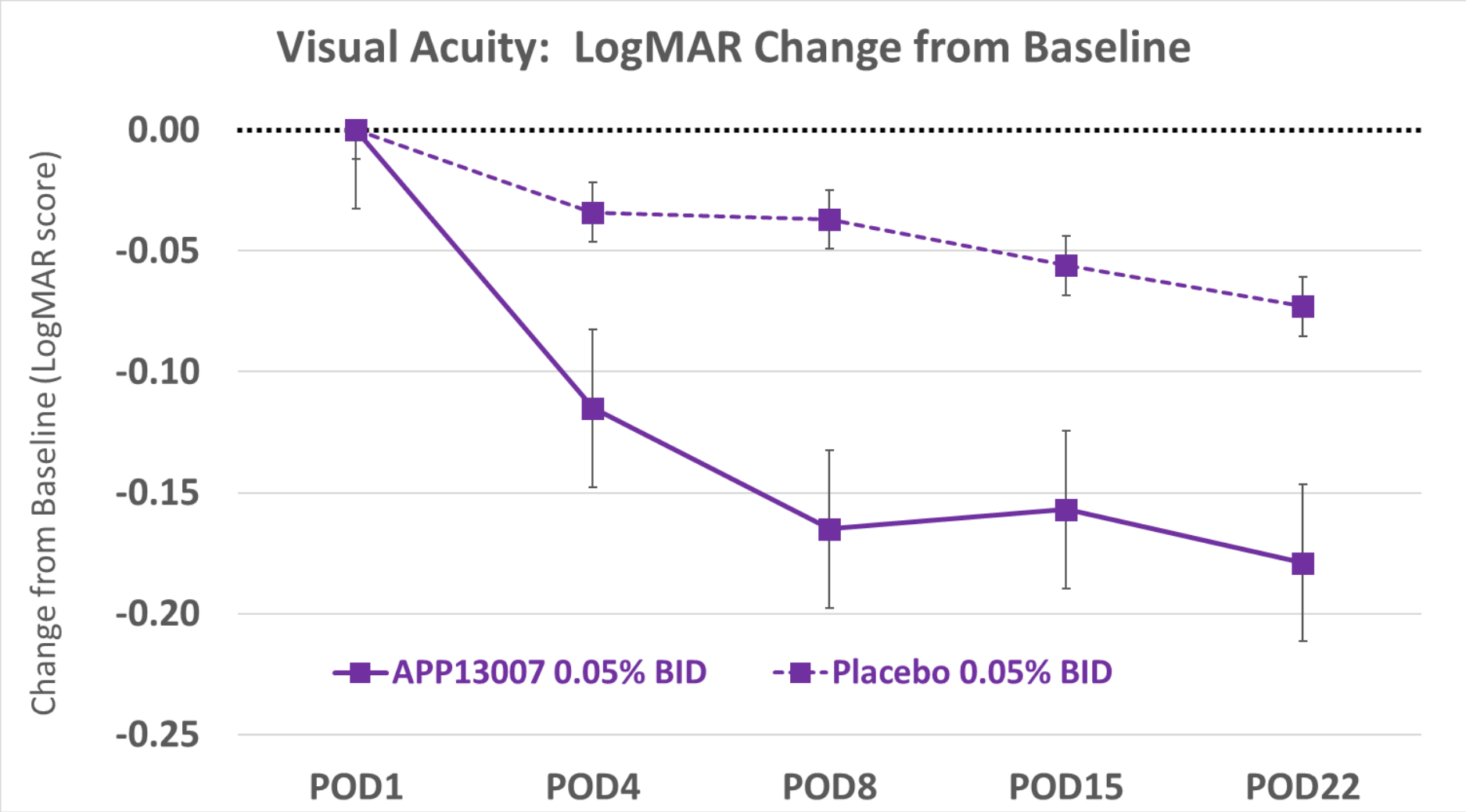
Sustained Pain Grade = 0

(sustained from POD4 to POD22 in Part A or POD15 in Part B)



Visual Acuity (LogMAR Score)

Mean Change from Baseline (± SEM)



Cumulative Number of Rescued Subjects – a marker of lack of efficacy

Day	APP13007 0.05% BID		APP13007 0.05% BID/QD		APP13007 0.1% BID/QD	
	Active	Placebo	Active	Placebo	Active	Placebo
POD 4	**0 (0 %)**	**1 (4.3 %)**	**0 (0 %)**	**4 (18.2 %)**	**0 (0 %)**	**4 (19.0 %)**
POD 8	**0 (0 %)**	**3 (13.0 %)**	**0 (0 %)**	**5 (22.7 %)**	**0 (0 %)**	**5 (23.8 %)**
POD 15	**0 (0 %)**	**3 (13.0 %)**	**0 (0 %)**	**5 (22.7 %)**	**0 (0 %)**	**5 (23.8 %)**
POD 22	**0 (0 %)**	**3 (13.0 %)**				

Pre-specified Rescue Criteria:

- After randomization, ACC count >30 cells.
- After randomization, an increase in ACC by > 15 cells from POD1 baseline.
- After randomization, ≥2 grade of increase in anterior chamber flare from POD1 baseline.

Summary of Efficacy

ACC Counts and Sustained ACC Grade = 0

- 0.05% APP13007 BID is superior to Placebo and may perform better than APP13007 BID/QD regimens

Ocular Pain Grade and Sustained Pain Grade = 0

- 0.05% APP13007 BID is superior to Placebo and may perform better than APP13007 BID/QD regimens

AC Flare

- Improvements are concordant with the ACC Count results

Visual Acuity

- Trend for rapid improvement with 0.05% APP13007 BID

Number of Subjects Rescued

- None on active APP13007, 13 on placebo

Safety – Adverse Events

APP13007 (APP) was well-tolerated with a safety profile similar to Placebo (PBO)

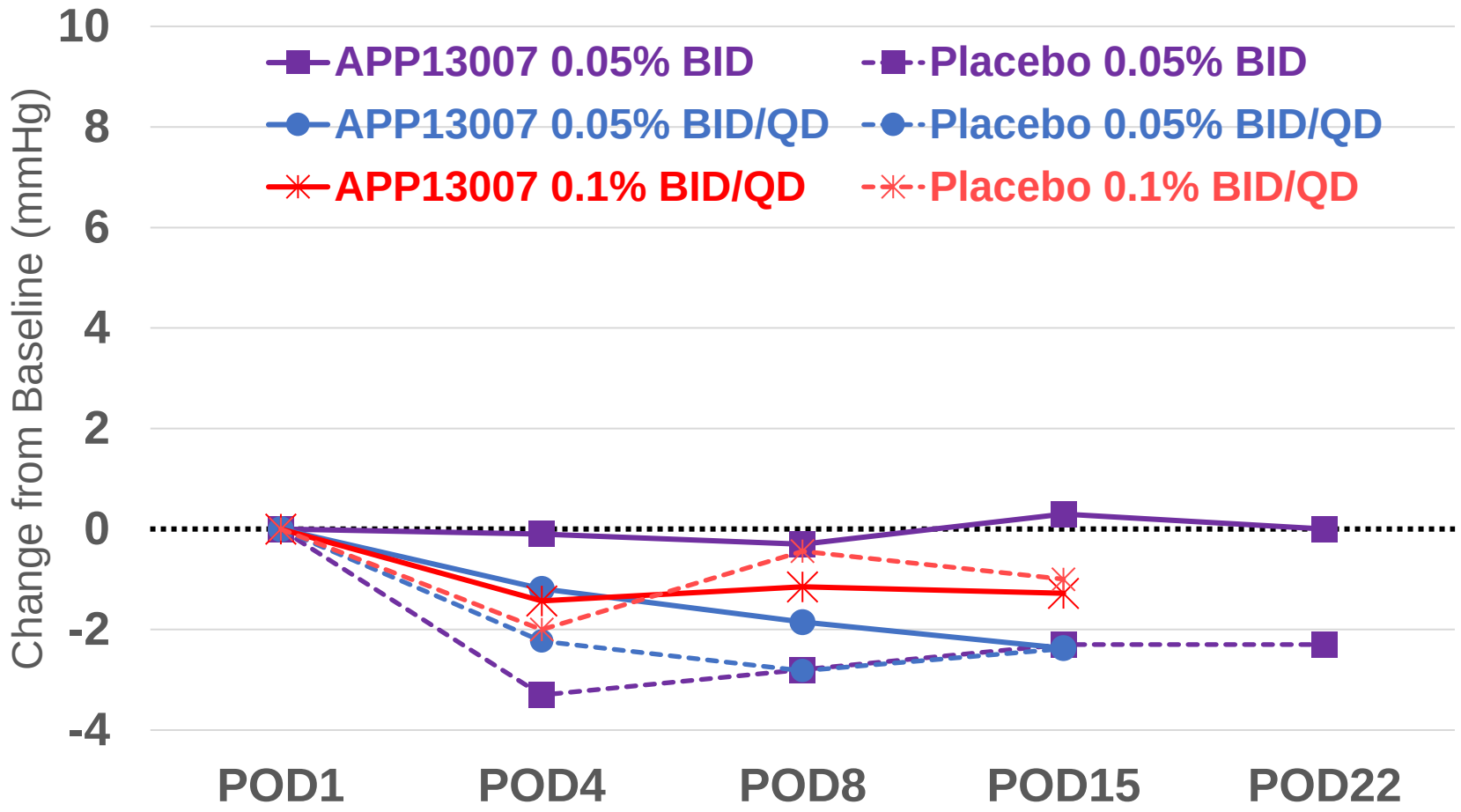
Part A	APP 0.05% BID (N = 22)		PBO 0.05% BID (N =23)	
Adverse Event	**N**	**# of Events**	**N**	**# of Events**
Eye Disorders (No irritation or grittiness)	2 (9%)	3	7 (30%)	10
Lab Safety Tests (present pre-dosing)	3 (14%)	3	0	0
Vomiting	1 (5%)	1	0	0
Eye Injury	0	0	1 (4%)	1

Part B	APP 0.05% BID/QD (N = 22)		PBO 0.05% BID/QD (N =22)		APP 0.1% BID/QD (N =22)		PBO 0.1% BID/QD (N = 21)	
Adverse event	**N**	**# of Events**	**N**	**# of Events**	**N**	**# of Events**	**N**	**# of Events**
Eye Disorders (1 PBO subject reported Foreign Body sensation)	3 (14%)	4	8 (36%)	10	5 (23%)	5	3 (14%)	5
Upper Respiratory Tract Infection	1 (5%)	1	0	0	1 (5%)	1	0	0
Headache	0	0	1 (5%)	1	0	0	1 (5%)	1
Cataract Surgery Complication	1 (5%)	1	0	0	0	0	0	0

Conclusion: No significant treatment-related adverse events

Safety – Intraocular Pressure

(Mean Change from Baseline)



Summary of Safety

Adverse Events

- No AEs related to APP13007
- No irritation or grittiness related to APP13007 formulations

Safety Lab Measurements

- No treatment-related effects

Intraocular Pressure (IOP)

- No treatment-related effects
- No meaningful difference between APP13007 and placebo
- No increase from baseline >10 mmHg

Conclusion

The safety and efficacy results from this study support the further clinical development of APP13007 0.05% BID for the treatment of inflammation and pain following ocular surgery

Acknowledgements

The authors and the Sponsor wish to thank the participating subjects and all the investigators who contributed to the conduct of this study

US Representative of Formosa Pharmaceuticals: AimMax™ Therapeutics, Inc.

Trial Sponsor: FORMOSA PHARMACEUTICALS, INC.