Iontophoresis Platform Safely and Effectively Delivers Dexamethasone to Manage Post Operative Inflammation and Pain Following Cataract Surgery.

JEFFREY H. LEVENSON, MD¹ (PRESENTING AUTHOR); BARBARA WIROSTKO, MD²; MICHAEL B. RAIZMAN, MD³

1. PRINCIPLE INVESTIGATOR FOR EYEGATE PHARMACEUTICALS (NASDAQ: EYEG)
2. CHIEF MEDICAL OFFICER, EYEGATE PHARMACEUTICALS,
3. CONSULTANT FOR EYEGATE PHARMACEUTICALS,
Purpose:

- To assess the safety and efficacy of a novel and proprietary iontophoretic platform, EGP437, in its ability to deliver dexamethasone to patients following cataract surgery.

- This technology offers the potential to control pain and inflammation after cataract surgery without the need for daily drop therapy.
**Iontophoresis Platform: A Non-Invasive Method of Propelling Charged Active Compounds Into Ocular Tissues**

- Small electrical current (constant); current has same charge as active substance (drug)
- Electrode creates repulsive electromotive forces (like charges repel)
- Drug migrates toward return electrode, mobility a function of molecular weight and charge
- Drug dose controlled by 2 variables: Current (mA) x Application time (minutes)
- Software-regulated current and duration ensures proper dosing of compatible compounds
- Easy to use: ophthalmologist or optometrist in <5 minutes
- More than 2,400 treatments performed in office settings

![Diagram of EyeGate Applicator and Current Pathway]
Ocular inflammation and pain are common side effects following cataract surgery

- > 24 million people age 40 and older have cataracts in the US
- Nearly four million cataract surgeries are performed each year in the US\(^1\)

Positive outcome from Phase 1b/2a, 80 subject open-label dose ranging trial

- Subjects enrolled into cohorts (10 subjects/cohort)
- Primary outcomes:
  - Proportion of subjects with anterior chamber cell (ACC) count of zero and
  - Proportion with pain score of zero

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Methods:

- A 28 day multicenter, open label trial enrolling up to 80 subjects who underwent unilateral cataract extraction with a monofocal intraocular lens.

- The trial design included 8 cohorts whereby 40 mg/ml of dexamethasone in iontophoretic doses of 4.0 mA min, 4.5 mA min, 9.0 mA min and 14.0 mA min were employed versus placebo;

- 9.0 and 14.0 mA min Cohorts included 3 different dosing regimens.
  - Subjects in the 9.0 and 14.0 mA min cohorts had three treatments administered starting day 0 (post surgery), day 1 and day 2 OR day 0 (post surgery), day 1 and day 4 with potential for an additional treatment at Day 7.

- A 9.0 mA min cohort also evaluated 30 – 60 minutes pre surgery day 0 dose followed by day 1, and day 4.

- The primary endpoint for all cohorts was ACC at day 14,

- Secondary endpoints included:
  - measuring pain score
  - Intraocular pressure
Results:

- A positive response was observed in the majority of the patients. The cohorts receiving the 4.5 mA min and the 14 mA min dose of iontophoretic EGP437 on days 0, 1 and 4 generated the most encouraging results, with an Anterior Chamber Cell count (ACC) of zero in 20-30% of patients at day 7 and 70-80% of patients at day 28.

- Procedure was very well tolerated with minimal pain throughout the duration of the trial.

- 8 of 10 subjects rescued by Day 4 in placebo arm – i.e. control arm for registration trials.

- Percentage of patients in 4.5 and 14 mA-min doses with zero pain on day 1 was 70 and 90% respectively.
Efficacy Results:

*Durezol data from CDER Application Number 22-212: Medical Review for Durezol, studies ST-601A-002a and 002b. Durezol data shown is based on combined data from both studies. QID dose, ITT, LOCF.
EGP-437 data from 4.5mA-min and 14mA-min dosed on Days 0, 1, and 4 (some subjects received additional dose at Day 7) and is ITT, LOCF.
Safety Results:

- No increase in IOP due to EGP-437
- In the two dose cohorts selected
  - Mild / moderate AEs included “expected” post operative findings, all of which resolved:
    - Excessive inflammation (30% in 14.0 mA-min & 0% in the 4.5 mA-min)
    - Corneal edema (50% of the 14.0 mA-min & 0% in the 4.5 mA-min)
    - Eye pain / Foreign body sensation (50% in 14.0 mA-min & 30% in 4.5 mA-min cohorts)
    - Mild transient eye or brow discomfort during procedure was noted in a minority of patients
  - On average Moderate inflammation was noted in the majority of the placebo group as expected which resulted in early rescue
Conclusions:

- EGP-437 is safe and effective in reducing inflammation and preventing pain as early as Day 1 with 2 different iontophoretic doses.
- Best responses observed with 4.5 mA-min and 14.0 mA-min doses
- Percentage of patients with ACC count of zero greater than Durezol historical data at Day 7 and Day 28
- Percentage of patients with zero pain better than Durezol historical data at Day 4, 7, and 14
- Phase 2b trial initiation targeted for 1H 2017

EGP-437 effectively controls post operative pain and inflammation without the need for drop therapy