NONCLINICAL EVALUATION OF NCX 4251, A NOVEL STEROID THERAPY FOR BLEPHARITIS, TARGETED DIRECTLY TO THE EYELID MARGIN TO IMPROVE EFFICACY AND REDUCE THE POTENTIAL FOR IOP ELEVATIONS

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REFERENCES
2. Internal estimate based on IQVIA Health Analytics data, 2017
5. Subject to successful completion of formulation and IND-enabling non-clinical studies

BLEPHARITIS: AN UNMET MEDICAL NEED

• Just like dry eye 15 years ago, blepharitis is poorly understood
• No U.S. FDA-approved product to specifically treat blepharitis
• Annual U.S. revenues of standard-of-care treatments (topical steroids, antibiotics and their combinations) total more than $100 million
• Blepharitis encountered by 37% and 47% of all patients seen by ophthalmologists and optometrists in U.S.
• The incidence of blepharitis is similar or higher than dry eye in a survey of patients with symptoms (24% blepharitis, 21% dry eye)
• Ophthalmic practitioners consider anti-inflammatory activity the most important product attribute to selecting a blepharitis treatment

METHODS

NCX 4251 - OPHTHALMIC SUSPENSION OF FLUTICASONE PROPIONATE NANOCRYSTALS

• Targeted topical treatment of the eyelid margin for patients with acute exacerbations of blepharitis
• Selected fluticasone, which is broadly used outside of ophthalmology, and is a ten-fold more potent molecule on the glucocorticoid receptor than dexamethasone
• Applied via an eyelid applicator at the eyelid margin directly to the site of inflammation to potentially decrease steroid induced ocular adverse events often seen with steroid eye drops
• U.S. IND submitted in Q4 2018 following a positive pre-IND meeting with U.S. FDA (U.S. patient coverage to 2033)
• Planned U.S. multi-center, Phase 2 study to evaluate safety and tolerability of NCX 4251 versus placebo

FLUTICASONE PROPIONATE MOLECULE - KEY PROPERTIES

• Fluticasone propionate (FP) binding affinity for glucocorticoid receptor (GCR) is 500 fold higher than dexamethasone and 20 fold higher than triamcinolone
• The rate of association with GCR is faster and the rate of dissociation is slower than other steroids
• FP is 1000-fold more lipophilic vs. triamcinolone and binds in tissue strongly and strongly
• The resulting half-life of the FP-GCR active steroid complex is >10 hours
• FP interferes with transcription factors that activate inflammation and vaso-relaxation

RESULTS

7-DAY REPEATED DOSE TOXICITY STUDY OF NCX 4251 OPHTHALMIC SUSPENSION IN BEAGLE DOGS

Study Design – Material and Methods

• Route: Dosing by eyelid applicator directly to the upper and lower eyelids of both eyes
• Frequency: Twice daily (BID), minimum of 6 hours between doses for 7 consecutive days
• Test system: Beagle dogs, approximately 5 months and weighing 6.6 – 9.1 kg for males and female on Day 1

RESULTS

14-DAY REPEATED DOSE TOXICITY STUDY OF NCX 4251 OPHTHALMIC SUSPENSION IN BEAGLE DOGS

Study Design – Material and Methods

• Route: Dosing by eyelid applicator directly to the upper and lower eyelids of both eyes
• Frequency: Once daily (QD) or twice daily (BID), minimum of 6 hours between doses for 14 consecutive days
• Test system: Beagle dogs, approximately 5 months and weighing 6.6 – 9.1 kg for males and female on Day 1

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CONCLUSIONS

NCX 4251 - OPHTHALMIC SUSPENSION OF FLUTICASONE PROPIONATE NANOCRYSTALS

• NCX 4251 is based on fluticasone, ten-fold more potent than dexamethasone, and targets the topical treatment of the eyelid margin for patients with acute exacerbations of blepharitis
• NCX 4251 is applied via an eyelid applicator at the eyelid margin directly to the site of inflammation to potentially decrease steroid induced ocular adverse events often seen with eye drops
• NCX 4251 was evaluated in 7-day non-GLP toxicology study and 14-day GLP toxicology study
• There were no dose limiting toxicology findings and no IOP increases, thus enabling the highest dose tested in toxicology studies to proceed into Phase 2 clinical study

IND in effect for forthcoming first-in-human, randomized, placebo-controlled Phase 2 clinical study in the U.S. to evaluate safety and tolerability of NCX 4251 vs placebo

Top-line results expected in Q4 2019

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