Long-acting in-situ forming implant with EP055 for non-hormonal male contraception

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INTRODUCTION

Due to the limited options for male contraception, we can develop a long-acting (LA) injectable in-situ forming implant (ISFI) with a novel non-hormonal male contraceptive, EP055. If we can successfully optimize EP055 ISFI to achieve a target in vitro release rate for 30 days or longer, then this study’s findings can be translated towards in vivo studies and clinical trials. With this translational technology, we can expand male contraceptive options and make a global impact in the family planning landscape.

Unmet Needs

- Nearly half of all pregnancies are unintended
- Only approved male options: Vasectomy and Condoms
- 28% of men use regular male contraception

Nearly half of all pregnancies are unintended, each year.

EP055

- Targets epididymal protease inhibitor (EPPIN)
- Rapid, reversible inhibition of sperm motility in rhesus macaques
- Short plasma half-life (~10.3 minutes)

In-situ forming implants (ISFIs) offer injectable, sustained drug release technology

ISFIs combine a biodegradable and hydrophobic polymer, water miscible organic solvent, and an active pharmaceutical ingredient (API) in a syringable suspension

ISFI will undergo phase inversion upon injection into subcutaneous space, generating depot

METHODS

- In-situ forming implants (ISFIs) offer injectable, sustained drug release technology
- ISFIs combine a biodegradable and hydrophobic polymer, water miscible organic solvent, and an active pharmaceutical ingredient (API) in a syringable suspension
- ISFI will undergo phase inversion upon injection into subcutaneous space, generating depot

Drug Release Optimization

- Release can be optimized by altering concentration and properties of formulation components
- Polymer: Poly[(acetic-co-glycolic acid) (PLGA)
- Solvents: NMP (N-methyl-2-pyrrolidone), DMSO (dimethyl sulfoxide), Benzyl Benzoate
- Depots were incubated in PBS + 2% Solutol at 37°C and aliquots were collected at predetermined time intervals
- Drug concentration and stability were quantified by high performance liquid chromatography (HPLC) analysis

RESULTS

Extended Release

Burst Release

Most Viable Formulation (.04)

CONCLUSION AND FUTURE DIRECTIONS

- Incorporation of the hydrophobic solvent Benzyl Benzoate reduces initial burst release and increases release duration
- Too much Benzyl Benzoate causes undesirable phase separation
- Too little Benzyl Benzoate has too quick phase transition
- Met EP055 target release rate (26-52μg/day) for over 30 days
- Can investigate different PLGA molecular weights, various polymer to solvent ratios, and change co-solvent ratios to fine-tune release kinetics
- Can transition to in-vivo studies to further test viable formulations

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REFERENCES


