Six Month Progress Report – AMMA Therapeutics

Development of a Once Daily Subcutaneous Injection of Cysteamine Bitartate

The project is comprised of 3 specific goals ("AIMs") conducted over a 1 year time period. In Summary:

AIM #1 (6 months): formulation development and in vitro testing

AIM #2 (3 months): small animal pharmacokinetic ("PK") testing

AIM #3 (3 months): small animal efficacy and safety testing

Accordingly, the first 6 months have been dedicated to completing AIM #1. We faced significant Covid 19 related disruptions to workflows and higher costs, but we have managed to stay within the projected timelines and budgets.

For AIM #1, we screened and assessed physiochemical properties for numerous BAIT formulations comprising different BAIT constructs. While our primary goal has been to develop a BAIT formulation of cysteamine bitartate, we also evaluated another form of cysteamine that may allow us to deliver greater amounts of cysteamine in smaller injection volumes. AIM #1 activities have been largely completed and we selected the most promising BAIT formulations to advance to Aim #2.

AIM #1 Goals	**Status**
1. Evaluate the solubility, chemical, and physical stability of Cysteamine Bitartrate in BAIT NPT formulation excipients. 2. Screen BAIT constructs that may comprise formulations that achieve optimal drug delivery profiles, stability, and applicable as subcutaneous injections.	1. Solubility – Completed 2. Compatibility – To be completed 3. Invitro drug release - Completed 4. Syringe injectability - Completed

The goal of AIM #2 is to select a single BAIT formulation, based on rodent PK studies, to advance to a longer-term efficacy study in AIM #3. Upon more comprehensive discussions and planning for AIM #3 with our scientific and project collaborators, Dr Rega and Dr Emma, it became apparent that 2 important unknowns could pose a challenge towards a successful AIM #3:

- The plasma cysteamine levels needed to achieve the desired efficacy in the cystinosis rodent model
- The proper dosing regimen (dosage, frequency) for cysteamine BAIT that achieves therapeutic plasma cysteamine levels

To elucidate these unknowns, AIM #2 has been expanded to include additional rodent PK and pharmacodynamic studies. It is our intention to stay within the project timelines and budgets despite the expansion of Aim #2. The first of these studies, a single dose PK study at AMMA, was initiated early February and we are awaiting bioanalysis results.