**DISEASE BACKGROUND**

- Congenital Adrenal Hyperplasia (CAH) is a rare genetic disorder with an estimated prevalence in the US and Europe of approximately 1:15,000 live births.
- The most common type of CAH is due to 21-OH deficiency caused by pathogenic variants in the CYP21A2 gene.
- Disease- and treatment-related complications include fetal/infantile crises, impaired growth and development during childhood, adult short stature, female virilization, infertility in both sexes, obesity and cardiovascular disease risk factors, and decreased bone mineral density.
- The all-cause mortality rate in classic severe CAH has been reported as >5 times that of controls, adjusted for age and sex.
- Classic (severe) CAH requires lifetime GC ± MC replacement.

**STUDY BACKGROUND**

- Gene therapy with BBP-631 is intended to restore adrenocortical cell function with the potential to reduce burden and improve chances of participants ultimately being enrolled in the investigational gene therapy trial.

**SPECIAL PROGRAMS**

- Immunogenicity testing for anti-21-OH and anti-viral vector antibodies.
- Increased chances for participants ultimately being enrolled in the investigational gene therapy trial.

**CAH-300 PRE-Screening Study Design**

**Immunogenicity & Genetic Screening**

**Flow Diagram of Study Participants in the CAH-300 Pre-screening Study**

**CONCLUSIONS**

- In addition to several other sources for identifying participants for the CAH-301 investigational gene therapy trial, the CAH-300 Pre-screening Study has enrolled 24 participants and enabled the efficient identification of multiple potentially eligible participants.
- Potentially eligible participants for the CAH-301 investigational gene therapy trial have baseline profiles that will allow for detection of increased cortisol production (as well as decreased 17-OHP) after administration of gene therapy, and have baseline profiles that will allow for detection of increased cortisol production (as well as decreased 17-OHP) after administration of gene therapy.
- Based on participants with available values (n = 13), cortisol (IA) levels are consistent with classic CAH and suggest potential eligibility participants for the investigational gene therapy trial.
- Morning cortisol levels measured by LC-MS/MS and IA are consistent with classic CAH.