**SUPPLEMENTARY METHODS**

*Safety procedures*

A number of safety procedures were established in the study, including the exclusion of people with recurrent episodes of fainting or hypokalaemia at screening, ensuring adequate fluid intake and replacement of fluid losses during and after the study, and provision for intravenous infusion of 0.9% NaCl in participants who developed hypotension, or who experienced a profound diuresis and were unable to maintain oral fluid intake. Blood pressure was monitored at each data collection time-point throughout the study period.

*Sample size calculation*

Although there were two co-primary hypotheses in this study (*SLC2A9* and *SLC22A11*), it was proposed that each would be treated independently with no adjustment for multiplicity (ie. alpha was 0.05 for each). In practice, recalculation of the sample size with alpha set to 0.025 (0.05/2, ie. *P* split between the two primary hypotheses) increased the difference that could be detected by 0.1 - a relatively trivial amount. As the primary analysis was based on the change from baseline, no adequate estimate of the variability of this was available and so the conservative approach of modelling the difference between-groups at a single time-point was chosen to validate the sample size. Sample size calculations were performed using PASS 2002 (Hintze, J (2006) Kaysville, Utah).

*Statistical analysis*

Differences in baseline participant characteristics between ancestral groups were analysed using t-tests for normally distributed data and Fisher's exact test for categorical data. Mixed model one-way analysis of variance (ANOVA) with Dunnett's multiple comparison test was used to analyse changes from baseline over time in the entire group. Pearson correlation and

stepwise linear regression was used to identify variables that were independently associated with changes in FEUA and serum urate at 60 and 180 minutes following frusemide intake. Variables with $P<0.05$ in the correlation analysis were included in the regression analysis. For the dependent variables measured at 60 minutes, only variables measured at 60 minutes were included in the regression model. $P<0.05$ was considered significant and all tests were two-tailed.