Introduction
Preclinical blood glucose testing methods have relied largely on human consumer market technology. The FDA accuracy requirement for consumer meters of ±20% is not ideal for research applications. Glucose strip measurements are known to be impacted by the level of hematocrit, the age of the blood, the hematocrit level, size of red blood cells, and distribution of glucose in plasma vs red blood cells can vary across animal models, and the hematocrit level can further be altered based on animal condition and drug interventions. The StatStrip® Xpress™ GLU meter (Nova Biomedical) provides increased accuracy by measuring and correcting for hematocrit values and is also immune to common interferents such as ascorbic acid and acetaminophen. The StatStrip meters have historically only been marketed for use in hospital settings, but are now available through Data Sciences International (DSI) for use in preclinical applications. The AlphaTRAK® (Abbott) meter has been used by PreClinOmics in past studies and is specifically marketed for preclinical use and has demonstrated higher accuracy in animal models than consumer meters. The present study compares both systems to the model AU480® (Beckman Coulter) Chemistry System.

Materials and Methods
Normal and diabetic ZDS rats (N=98) were used to evaluate the performance of the StatStrip and AlphaTRAK glucometers against the AU480. The StatStrip meter used is an “investigational use only” meter that has been modified by Nova Biomedical and provided by Data Sciences International to accommodate a range of 10-900 mg/dL rather than the standard 10-600 mg/dL for the human model. Controls were run on each glucose meter making sure that all of the controls were in the target range. Each rat was removed from its cage and the tail cut and bled (80-100 µL) into a lancing tube to be used for the AU480. The rats were then passed to another person who bled them into the glucose meter strips. A third person was writing down the measured values. Two meters of each type were used and two measurements were made with each of the type meters for each time point of data collection, and whenever possible the same drop was used for all four strips. This process took three hours starting at 9:02. The two measurements were averaged for comparison across analysis methods. The tubes were kept in a cold block until post analysis start- ed at 12:43 and continued until 14:38. Blood was well mixed before running it on duplicate samples for each meter a second time using a single pipette of blood in the same sampling sequence. The same sample of blood was spun in a refrigerated centrifuge three hours starting at 9:02. The two measurements were averaged for comparison across analysis methods. The GO GTI test drove glucose values to nearly 800 mg/dL (total N=60) and this data was added to the dataset. The StatStrip meter performed well with R² = 0.99, slope = 0.94 and offset = +4.9. The difference in slope and offset from our other study results seen on the AU480 in four separate measurement groups.

Results
Our results will focus on the comparison of the afternoon strip measurements and the AU480 analysis results (Fig 5). The AlphaTRAK results showed a bias of -9.0% relative to the AU480 with a range of glucose studied of 10-900 mg/dL. The StatStrip results showed a bias of +5.6% relative to the AU480 with a zero crossing of -10.1 mg/dL. The R² value was slightly better for the StatStrip readings at 0.993 versus 0.966 for the AlphaTRAK. The average absolute difference between the AlphaTRAK and AU480 was 15.3% for the morning and 8.1% for the afternoon measurements. The average absolute difference between the StatStrip and the AU480 was 5.4% for the morning and 4.7% for the afternoon measurements (Table 1).

We evaluated the duplicate samples for each of the initial meter measurements. Both the StatStrip and AlphaTRAK showed high correlations of R²=0.99 (Fig 6) as well as average errors within about 4%. There were two instances where there was a negative bias to, and statistically significant difference between, sample two vs sample one as seen in Table 1. One instance involved the AlphaTRAK meter (afternoon tube sample) and the other involved the StatStrip meter (morning fresh blood sample). The average absolute difference between the first and second readings was 3.5-4.2% for StatStrip and 2.3-3.0% for AlphaTRAK in three separate measurement groups.

Discussion
We don’t have an explanation for the statistically significant differences between two sequential samples seen on one dataset each for StatStrip, AlphaTrak, and AU480. We used the same lot of strips, so we don’t suspect a variation between strip lots. It is possible that there were differences between the duplicate meters of each type, but this didn’t show up consistently. While the differences were test huge (-1.7% to +1.0 bias), the statistical significance of the differences is puzzling.

Further investigation is needed to determine whether the higher afternoon values were a result of the plasma glucose levels changing between samples. Preclinical studies are needed to investigate whether there are other unknown influence on the measurement system(s). The difference in magnitude between the devices and StatStrip might also be explained by these further studies.

Summary/Conclusion
Both meters provided very good correlations with the AU480 across the range of study conditions. The StatStrip system provided more accurate data than the AlphaTRAK system and data nearly equivalent to the AU480 clinical analyzer over the range of glucose studied. Importantly the StatStrip introduced less bias to the morning and afternoon measurements relative to the AU480. PreClinOmics has elected to standardize on the StatStrip to take advantage of the improved accuracy for preclinical research studies. The ability to perform up to 900 mg/dL will provide significant benefit for research studies involving glucose challenges.

We found that timing of analysis relative to the blood sampling had a significant impact on the values obtained, and that it is important to analyze the same blood sample at the same time in order to correctly compare analysis methods. Follow up studies will be considered to further assess the impact of timing of analysis relative to blood sampling and factors contributing to error/bias.

References