UNMET NEED:
ICH E14 mandates a dedicated study for essentially all small molecules to assess the risk of QT prolongation on the ECG that can lead to potentially fatal cardiac arrhythmias. For most companies, these thorough QT (TQT) studies are expensive and a challenge for sponsors to perform. Traditional TQT core labs have realized the implementation of cost effective approaches for ECG processing in TQT studies. We present a comprehensive plan to simplify planning, bidding, contracting, and executing of TQT studies while markedly decreasing overhead and ECG processing costs by about 50%. By reducing the cardiologist review by about 90%.

PROPOSED SOLUTION:
Based upon experience working with all the major ECG core labs in 36 TQT studies and over 140 Phase I studies with intensive ECG monitoring, Celeron has identified three areas where costs efficiencies could be realized while maintaining or increasing data quality. These areas are hybrid Phase I ECG Core lab formation, equipment selection and ECG processing.

Potential Commercial Markets: All nonsmall, small molecule compounds in development targeting FDA approval.

Potential Collaborators: AMPS, LLC and Global Instrumentation

SUMMARY:
Celeron has developed a Hybrid Phase I ECG core lab that minimizes overhead and utilizes bluetooth Holter monitors that eliminate the need for stand alone ECG machines and decreases data entry errors. This highly automated approach to ECG analyses not only decreases costs significantly, but also preserves the ability to analyze the potential for smaller TQT sample sizes and further savings to sponsors. The FDA approved no concern using this system in a TQT study provided an appropriate moxifloxacin effect was seen, a requirement for any TQT study regardless of the measurement method used.

Figure 1: Antares® Optimal ECG Extraction. The time window selected around nominal time point is at the top. On the left side the preceding HR and artifact level are acceptable. On the right side at the nominal time extraction there is significant preceding HR instability and artifact. Decreasing HR instability and artifact decreases variability.

Figure 3: Change in baseline adjusted, placebo extracted (so-called double delta) moxifloxacin effect on QTcF interval in Celeron trial. Note typical magnitude and time course of the drug effect. For a TQT study to be judged adequate by the FDA, the moxifloxacin effect must have a lower 95% confidence intervals (CI) greater than 5 ms (red dashed line) around maximal effect. At 24 hours moxifloxacin effect has decreased to 5 ms. At the 5 ms effect level this study would be able to exclude a upper 95% CI of 10 ms (green dashed line), the criteria for a positive study.