



# AnaBios

Early Human Insights

## CASE STUDY

### ***Predicting Heart Rate Effects on Ex Vivo Human SA Node***

A drug in preclinical development for atrial fibrillation had no measurable activity in hERG, Nav1.5 and Cav1.2 channels. Preliminary tests in guinea pigs appeared to confirm lack of potential cardiac risks, while a dog telemetry study confirmed the absence of drug-induced pro-arrhythmia markers. However, a significant increase in heart rate found in the dog telemetry study halted the program due to concerns about blood clotting and stroke risk in patients.

Utilizing Phase X<sup>®</sup> technology, AnaBios evaluated the heart rate-related risk of the compound in a human ex vivo sino-atrial (SA) node model. This unprecedented preparation detects both positive and negative chronotropic effects of drugs by recording the pacemaker activity of the human SA node. The molecule exhibited no measurable chronotropic effects, while positive (isoproterenol) and negative (carbachol) chronotropes exhibited the expected activities.

Unfortunately, species differences in drug-induced chronotropic effects are often observed in drug development programs. Ultimately, this study suggests animal models pose significant challenges in predicting drug-induced heart rate changes in humans. The availability of the human ex vivo SA node preparation opens up new opportunities for assessing this class of toxicities at an early stage in drug development.