Draft Agenda: New Advances in the Assessment of Drug-Induced Arrhythmias and the Comprehensive In Vitro Proarrythmia Assay (CiPA)

May 21-22, 2018

DAY 1

8:00 am **Continental Breakfast**

Welcome and Introduction
Review of the agenda and meeting goals

8:15 am **Overview**
Moderator: *Norman Stockbridge, US FDA*

- TdP mechanisms and insights - scientific rationale for CiPA [*Gary Gintant, AbbVie*] (15 min)
- The need for a new approach to assessing the proarrhythmic potential of drugs and overview of CiPA [*Philip Sager, CSRC*] (15 min)
- The potential role of CIPA on drug discovery, development, and regulatory pathways [*David Strauss, US FDA*] (20 min)
- Q&A/Panel discussion (Krishna Prasad (EMA), Corina Dota (AstraZeneca), Peter Kowey (Jefferson Univ), 40 min)

9:45 am **Break**

10:00 am **In Silico Modeling and Ion Channel Approaches**
Moderator: *Gary Mirams*

- In Silico modeling- state of the art [*Gary Mirams, University of Nottingham*] (15 min)
- Summary of In Silico model approach and validation study; In Silico Results [*Zhihua Li, US FDA*] (30 min)
- Ion Channel Assays and Data – lessons learned and data quality criteria [*Wendy Wu, US FDA*] (30 min)
- Q&A/Panel discussion (Speakers and Najah Abi Gerges, AnaBios; Jim Kramer (Charles River); Taka Yoshinaga (Eisai); 50 min)

12:00 pm **Working Lunch**

12:30 pm **IPS-Stem Cells and Phase 1 ECG**
Moderators: *Gary Gintant, AbbVie and David Strauss, US FDA*

- IPS-Stem Cells: Summary of approach, Detailed results and implications [*Ksenia Blinova, US FDA*] (30 min)

- New ECG biomarkers and their potential role in CiPA; Results and implications [Jose Vicente, *US FDA*] (30 min)
- Implementation of ECG biomarkers [*Borje Darpo*] (10 min)
- Q&A/Panel discussion (Yasunari Kanda (Japan NIH), and Charles Benson (Lilly); 50 min)

2:30 pm **Break**

2:45 pm **Regulatory Evaluation and Potential Implementation**
Moderator: Philip Sager

- Data summary overview [*Norman Stockbridge, US FDA*] (15 min)
- How CiPA might impact pre-clinical safety testing and S7B [*Derek Leishman, Lilly*] (15 min)
- How CiPA might be implemented in clinical development and regulatory decision making [*Christine Garnett, US FDA*] (15 min)
- Regulatory considerations and next steps [*Krishna Prasad, MHRA*] (10 min)
    - Q&A/Panel discussion (60 min) Including David Strauss, Colette S, Kaori Shinagawa, Chinese ICH Regulatory Member, Swiss ICH Regulatory Member, Jean-Pierre Valentin, Maki Ito

4:45 pm **Adjourn**

DAY 2

7:30 am **Continental Breakfast**

8:00 am – 10:30 am **Work Stream Breakouts**

Breakout 1 – In Silico (leaders: *Zhihua Li, US FDA; Gary Mirams, Lars* Johannesen *US FDA)*

Breakout 2 – Ion Channel (Wendy *Wu, US FDA; Jim Kramer, Charles River;* Najah Abi Gerges, AnaBios)

Breakout 3 – Myocyte (*Gary Gintant, ABBVIE; Ksenia Blinova, US FDA*; Yasunari Kanda (Japan NIH)

Breakout 4 – Phase 1 ECG (Jose Vicente, *US FDA; Christine Garnett US FDA)*

10:30 am **Break**

11:00 am **Reports from Work Stream Breakouts**

12:00 pm **Working Lunch**

12:30 pm Advances in Clinical QTc Assessments and Updates from the FDA QT Interdisciplinary Review Team (IRT)

Moderator: Philip Sager (Stanford University)

- Recent insights from the FDA QT IRT on Concentration-QTc analysis and requirements for obtaining a 'TQT study waiver' (Dhananjay Marathe, US FDA) 15 minutes
- Application of bias metrics during IRT review (Lars Johannesen (US FDA); 10 min)
- Issues with exposure-response analysis, how we can close the gap (Georg Ferber (Consultant); 20 min)
- QTc evaluation for drugs with a substantial heart rate effect (Marek Malik (University of London); 15 min)

Panel Discussion and Q&A (60 min) [Speakers and Christine Garnett (US FDA), Borje Darpo (ERT), Dalong Huang (FDA))

2:30 pm **Adjourn**