DruSafe Leadership Group
WG1: Nonclinical to Clinical Translational Database

Thomas Monticello
Vic Kadambi

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IQ Symposium 2014 – “Precompetitive Collaboration for Innovation”

WG1 Participants

IQ Company	WG1 Participant
abbvie	Matt Dieter
Allergan	Tim Maziasz
Amgen	Tom Monticello
Astellas	Marlowe Schneidkraut
AstraZeneca	Sean Redmond
BiogenIdec	Ken Loveday
blueprint	Vic Kadambi
BMS	Mark Tirmenstein
Boehringer	Victor Chen
Celgene	Jim Hartke
Daiichi Sankyo	Michael Pignatello
Eisai	Yvonne Van Gessel

IQ Company	WG1 Participant
Genentech	Donna Dambach
Gilead	Anne Chester
GSK	Tim Hart
Incyte	Claire Nielan
Infinity	Alex Constan
J&J	Michael DuVall
Lilly	Mark Carfagna
Novartis	Dan Lapadula
Pfizer	Mary Sommer; Mike Bolt
Sanofi	Mike Pino
Takeda	Andy Lynn
Vertex	Graeme Smith

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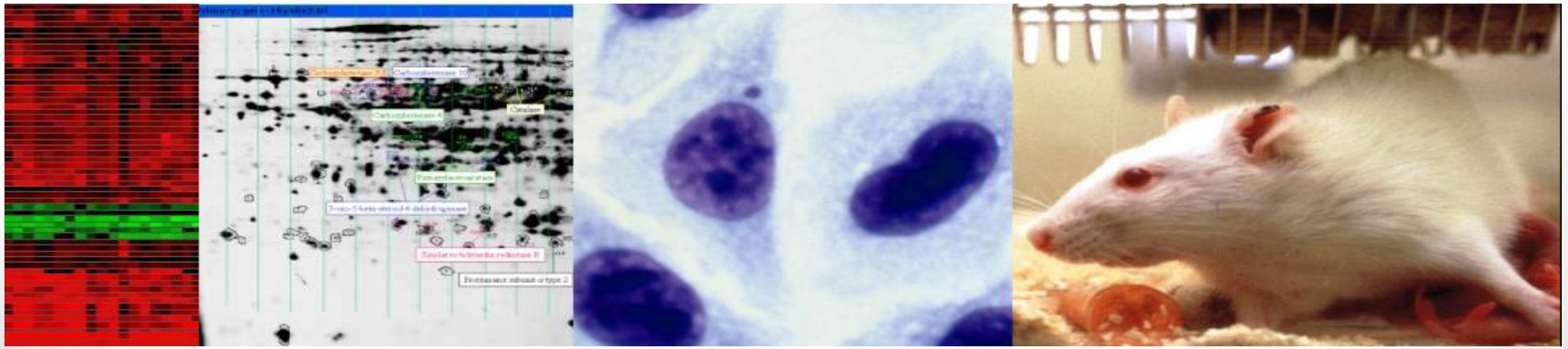
WG1: Background/Problem Statement

Goals of Nonclinical Safety Testing in Animal Models

- Ensure human safety in the clinic
- Determine safe starting dose
- Identify target organs of toxicity for clinical monitoring plan



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WG1: Background/Problem Statement

Current Testing Paradigm Based on Tradition and ICH Guidance

- Assumes current choice of animal models and study design are truly predictive of possible human hazard

- Limited publications exist, however, that scientifically address correlations between observed toxicities in animal models to those in the clinic

ICH
harmonisation for better health

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How did we get to WG1?

- Kicked off 1Q 2012 (WG rated highest priority by LG in 4Q11)
- Solicited companies to participate (currently n = 24)
- Created data entry spreadsheet
- Created database repository (BI support)
- Established 3rd Party Web Server for database (BI and IQ)
- Created Data Sharing Agreement (IQ)

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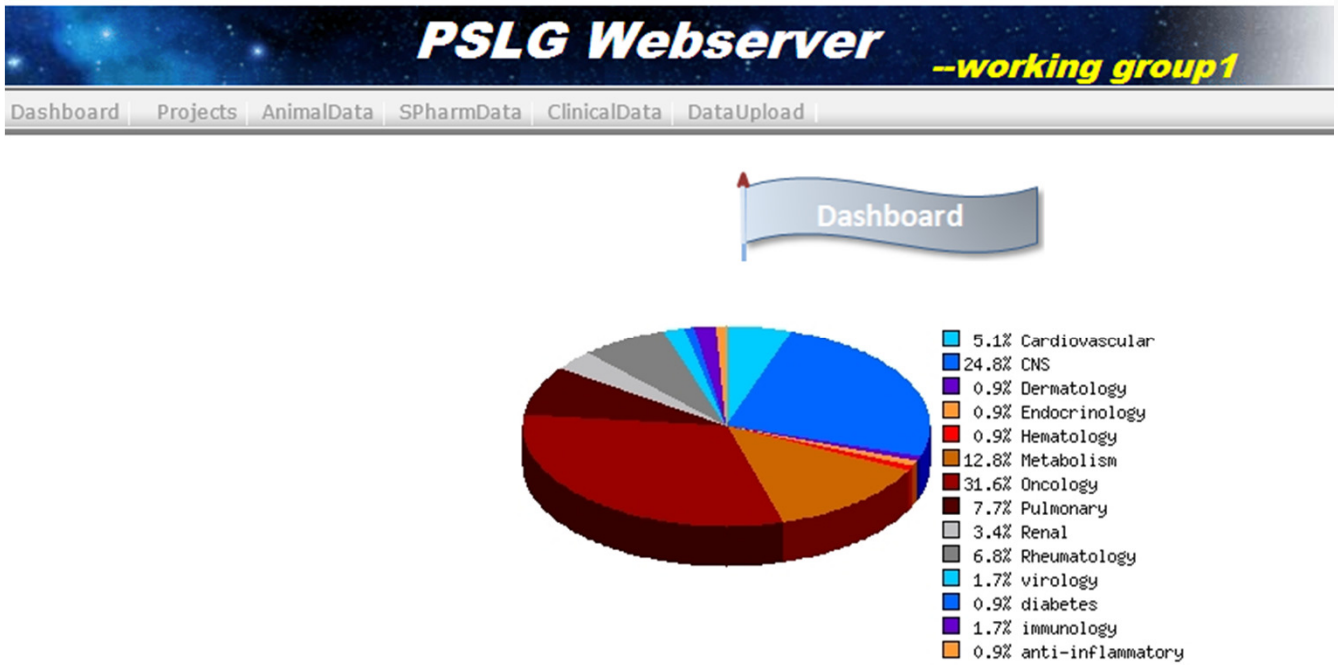
Where are we now?



- 110 molecules in database (Goal is 200 by EOY)
- Initial data quality review completed
- WG1 presented at national meetings (SOT, STP)
- WG1 initiative manuscript published (*Tox Pathol,* 2014)
- Publication of results 3Q15

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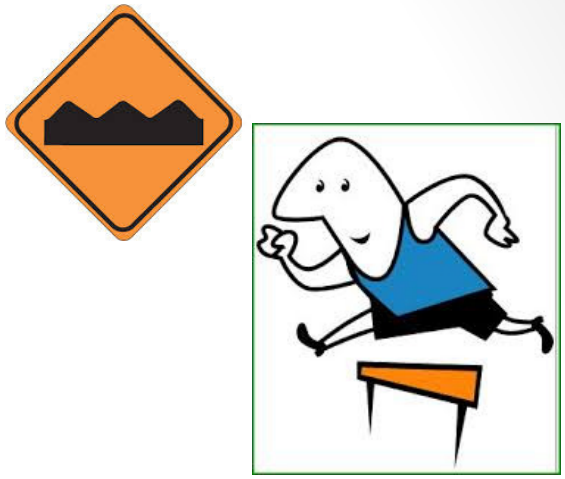
Lessons Learned (to date)

Bumps and Hurdles along the way……



Volunteerism is Critical and Must be Unwavering

- Delays in getting company buy-in
- Delays in getting legal approval
- Delays in assembling data in advance
- Delays in entering data
- Lack of resources to populate database and provide peer review

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Time Delays……

- to create the database tool
  - A first - unchartered territory [progress being made by IQ]
  - Success only because of BI commitment and support

- to finalize the IQ Data Sharing agreement
  - A first - [progress being made by IQ]
  - Difficult to appease Counsel for all participating companies

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Innovation through Precompetitive Collaboration- Summary

- WG1 creating a powerful database as a result of wide-based industry participation and collaboration
- WG aligns with the 2011 FDA strategic plan to advance regulatory science and modernize toxicology to enhance product safety
- WG dataset will aide in determining value of current testing paradigm
- Unique prospective database will continue to expand with longer duration nonclinical and clinical studies

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WG 1: Impact

- Precompetitive Collaboration, facilitated by the IQ, will help achieve our mission of advancing science-based and scientifically-driven standards to facilitate innovation in pharmaceutical development :

  - Value of both rodent and non-rodent approach?
  - Animal models predictors of human AEs?
  - Nonclinical safety study designs adequate?
  - Gaps in current state of safety biomarkers?
  - Excessive animal work beneficial (3Rs)?
  - Alternatives ? e.g. more 'humanized' testing approach

Thank You

Questions?