Sage Wikman – Business Development Manager
Absorption Systems
Thank you!

Institute for Scientific Communications, Inc.

Ms. Nola Mahaney & Team
Integrated Full Service CRO

**In Vitro / In Vivo / Ex Vivo** GLP and non-GLP services

**Discovery**
- Screening
- Lead Generation & Optimization

**Development**
- Drug-Drug Interaction Assessments
- Formulation & Advanced Permeation Evaluation
- Toxicity

**Specialty**
- Dermal, Ocular, Medical device testing
Augmenting Research

FDA & EMA Inspected

Drug discovery and development

*IND, NDA & BLA*

Product value enhancement

*505(b)(2)*

ANDA

*Solid oral & complex drug products*

510(K)

*Medical Device*
Absorption Systems Services Overview

Bioequivalence
- BCS Biowaivers
- Complex Drug Products

Drug Delivery
- Tissue Models

PK & Tox
- Small & Large Animal Mechanistic/Surgical

Ocular
- Efficacy & Safety
- PK & biodistribution

Medical Device
- Proof of Concept
- 510k Submission

Physicochemical
- ADME Profiling

Biochemical
- Metabolism
- Transporters
Small Molecule/ADME

NDA-enabling portfolio, Drug Discovery, Drug Development

- Permeability (CellPort Caco-2 and MDCK cell lines)
- Stability
- Metabolite Detection
- Enzyme Inhibition
- Protein and Tissue Binding
- Transporters
  - Substrate and/or inhibition
  - Efflux and uptake transporters
- LogD/Solubility
- Biopharmaceutical Classification System (BCS)
Compound Development

- Transporter Interactions
  - Test Systems
    - Caco-2
    - MDCK
    - LLC-PK1
    - Caco-2 Knockdowns
    - HEK293
    - Vesicles
  - Transporters
    - P-gp, BCRP, MRP2, OCT1, OCT2, OATP2B1, PepT1, BSEP, OATP1B1, OATP1B3, OAT1, OAT3, MATE1, MATE2K, ASBT

- CYP Interaction
  - Induction
  - Inhibition
  - Phenotyping
  - TDI

- Metabolism
  - *In vitro* Clearance
  - Metabolite ID
  - Metabolite Production
  - Non-CYP mediated
BCS Biowaivers

- Regulatory acceptance of *in vitro* testing as a reliable surrogate for *in vivo* bioequivalence study
- Cell-culture conditions approved by FDA on multiple audits
- 32 of the 36 approved Biowaivers were performed by Absorption Systems

Biowaivers granted for Class I and Class III drug substances
Includes highly variable drugs; not dependent on therapeutic class
Bioanalysis

- **Small Molecule**
  - LC-MS/MS
  - UPLC-MS/MS
  - Waters Xevo TQ-S
  - LTQ Orbitrap
- **Large Molecule**
  - ELISA
  - Immunoassays
  - Western Blot
  - Bioassay/ Cell Culture
  - Neutralization bioassays
  - Ligation assays (PLA)
- **Clinical bioanalysis**
- **GLP and Non-GLP**
- **Radiolicensed**
Large Molecule/Biologics

In-vivo, cell-based, and bioanalytical tests

- Cell Based Assays
- Proliferation Assays using various cell types
- Cell Viability and TCID50 titer
- Cytokine Release and Migration Assay
- GMP Lot Release Testing
- ELISA
- Quantitative Western Blot
- Enzyme Activity Assays
- Flow Cytometry
- Fluorescent and Luminescent Assay
- PCR
Potency Assays for Cell Therapy

- ACF
  - Supports regulatory requirements for validated potency assays
  - GMP production for batch qualification

- When we can help:
  - De novo assay development
  - Technology Transfer
  - Evaluation, Optimization, Modification
  - Qualification
  - Validation
  - Product Stability and Release testing
Tissue Models

- *Ex-vivo* site-specific absorption and formulation optimization
  - Ocular
  - Buccal
  - Sublingual
  - Intranasal
  - Oral
  - Transdermal
  - Intravaginal

- *In-Situ* Organ Perfusion
  - Liver
  - Brain
  - Intestinal
In Vivo Certifications & Accreditations

- AAALAC Accredited
- USDA, NIH registration
- OLAW Assured
- ISO Certified
- FDA-Inspected
- General Surgical Expertise
- IND Enabling Studies
- Model Development
- Custom Designed Programs
- Acute and Chronic Studies
- Non-GLP and GLP
- In Life and Bioanalysis
### Pharmacokinetic/Tolerability/Toxicity

#### Species
- Rat
  - Sprague Dawley
  - RNU
- Mouse
  - CD-1
  - C57BL/6
  - BALB/c
  - SCID mouse
- Dog
  - Beagle
- Rabbit
  - New Zealand White
  - Dutch-Belted
- Mini-pig
  - Yucatan
  - Gottingen

#### Dose Routes
- Intravenous (IV)
- Oral (PO)
- Subcutaneous (SC)
- Intramuscular (IM)
- Intraperitoneal (IP)
- Topical
  - Skin & Eye
- Sublingual (SL)
- Buccal
- Intraarticular (IA)
- Intranasal (IN)
- Intrathecal (IT)
- Intraduodenal (ID)
- Intracolonic (IC)
- Intrajejunal (IJ)

#### Sampling
- Blood/Plasma/Serum
  - Jugular vein
  - Portal vein
  - Other suitable veins
- Urine
- Feces
- Tissues
- Synovial fluid
- CSF

#### Tolerability/Toxicity Endpoints
- Clinical pathology
- Histopathology
Facilities
Ocular Services

PK, Toxicity, Efficacy, Devices, Disease Models & Custom Model Development

Posterior Segment
- ERG
- OCT
- FA
- Fundus Photography

Anterior Segment
- IOP
- Pachymetry
- Specular Microscopy
- Slit Lamp Biomicroscopy
Ocular Disease Models

VEGF Induced Vascular Leakage
- IVT injection of VEGF
- Fluorescein Angiography & Scoring to assess vascular leakage

Glaucoma
- Normotensive or hypertensive
- Evaluate IOP effect over time

Dry Eye
- Daily Atropine dose, increased airflow, and low (<20%) humidity
- Evaluation of Schirmir tear test, tear break up test, & fluorescein staining

Corneal Wound Healing
- Alcohol or NaOH (Alakali Burn)
- Evaluate wound area using slit-lamp photography
Medical Device Services

Metabolic Studies, Diabetic Models, Cardiovascular, Regenerative Medicine

- Vascular Grafts
- Deep Vein Thrombosis
- Mechanical Thrombectomy
- Angioplasty Procedures
- Venous Valve Transpositions
- Induced Myocardial Infarction
- Induced Aneurysm
- Stent Placement LVAD Implants
- Local Drug Delivery via PTCA Balloon
# Specialty Animal Models

## Lymph Collection

**Species**
- Sprague-Dawley Rat

**Dose Route**
- Various routes including oral gavage, and intraduodenal infusion (ID)

**Standard Formulations**
- Solution/Suspension

**Collection Site**
- Mesenteric
- Thoracic

**Outcome**
- Lymphatic Disposition

## Intraoral

**Species**
- Rabbit
- Rat
- Dog
- Minipig

**Standard Formulations**
- Dissolving films
- Sprays
- Gel
- Solution/Suspension

**Outcome**
- Comparing exposure to other administration routes and absolute and relative bioavailability

## Endoscopic & Surgical Gastrointestinal Dose Administration

**Species**
- Dog
- Minipig
- Rat (Surgical only)

**Dose Routes**
- Intraduodenal (ID) – endoscopic or surgical
- Intracolonic (IC) – endoscopic or surgical
- Intrajejunal (IJ) – surgical

**Standard Formulations**
- Liquid (ID & IC & IJ), Capsule (ID)

**Outcome**
- Regional absorption to assess GI effects on stability or as a barrier to bioavailability

## Dermal

**Species**
- Rat
- Guinea Pig
- Rabbit
- Minipig (Yucatan or Gottingen)

**Standard Formulations**
- Patch, Gel, Cream
- More

**Accumulation Assessment in Tissue**
- Punch Biopsies – varying sizes and depths

**Irritation Assessments**
- Modified Draize Scoring (Erythema and Edema)

**Outcome**
- Dermal and systemic disposition
Absorption Advantages

- Privately owned CRO
- Scientific expertise and operational excellence
- Analytics enabled, definitive test systems
- Dedicated Team
  - Dedicated Study Directors (PhD, DVM)
  - Board Certified Veterinarians
  - Highly trained Research Associates
  - Dedicated Study Managers
- Custom model development support
- State-of-Art Facilities
- Quality standards (GLP/ISO) and SOP’s
- Regulatory experience and oversight
- Cost savings, consistency, and logistical efficiencies
State of the Art in Clinical Transporter DDI Evaluation

Absorption Systems' hosted webinar with GlaxoSmithKline's Senior Fellow and Director of DMPK, Dr. Maciej J. Zamek-Gliszczynski, presents on recent research on DDI Evaluation:

- Transporters in drug development based on four recent International Transporter Consortium whitepapers
- Overview of emerging transporters of clinical relevance
- Best practice in design of clinical DDI studies through recent advances
- Consideration for optimal selection of clinical probe drugs, including future potential utility of transporter biomarkers

Download a Recording of the Webinar and Gain Access to all Four Whitepapers:

www.absorption.com/transporter-webinar
Thank you for your time!

Sage Wikman – Business Development Manager