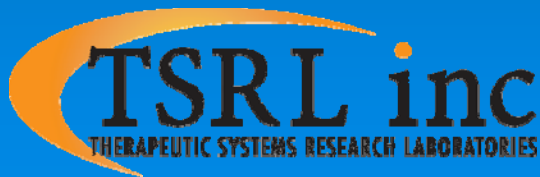


# Therapeutics Systems Research Laboratory (TSRL, Inc.)

## Technology and Service Capabilities

Elke Lipka, PhD, MBA

January 21<sup>st</sup> – 25<sup>th</sup>, 2008



# TSRL Mission

To be the premier partner to drug discovery companies for the joint development of novel patented oral drug delivery products to improve patient therapy.

We do this by applying our expertise in oral drug delivery and ADME/PK to our patented drug delivery technologies thereby creating customized product formulation solutions.

# Business Model

Product Inception

Commercialization

Internal R&D

ADME/PK  
Problem Solving

Business  
Development

Drug Delivery  
Solutions

Licensing

Strategic  
Partners

<http://www.tsrlinc.com/new/>

# Company Background

## ➤ Strong Research Team

- 6 PhD's, 2 Masters, out of 16 Total staffing
- 200+ years combined experience

## ➤ Founder: Gordon L. Amidon

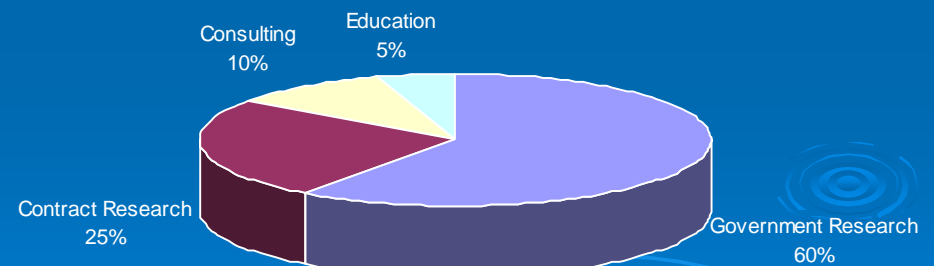
- Internationally recognized expert in the field of solubility, transport phenomena, prodrugs, and drug absorption.
- Developed the Biopharmaceutics Classification System (BCS) with the FDA, which serves as a basis for international drug regulation.

## ➤ Experts in oral drug delivery

- Consulting
- Education (MBcal, GastroPlus)

## ➤ Facility

- 5200 sq ft. (3700 sq ft wet lab space)
- Analytical Laboratories
- Tissue Culture Facility
- Synthetic Chemistry
- Biopharmaceutical Laboratory (AALAC accredited)



# TSRL Drug Delivery Strategies

## ➤ Characterize the Issue

- API/Drug Product:
  - Solubility
  - Dissolution
  - Stability
- In vitro / in vivo performance:
  - Intestinal Permeability (BCS), regional and composition dependent
  - Full PK/Bio
  - Metabolism
  - Exploratory toxicology

## ➤ Propose Delivery Solution

- Solubility enhancement
- Permeability enhancement
- Prodrug approach
- Time and rate controlled release technologies

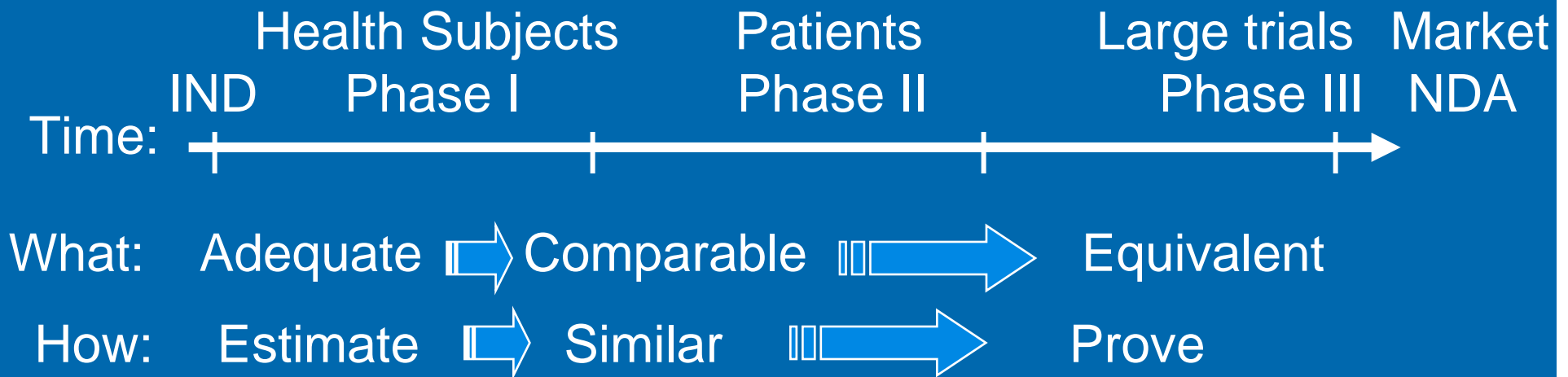
## ➤ Early Development Partners

- Formulation scale-up
- Long term stability
- Toxicology
- Phase I – Pharmacokinetic POC

# TSRL Preclinical Services

- Oral Drug Delivery Consulting
- Preclinical PK/ADME
  - In vitro cell based absorption & metabolism
  - GLP and non-GLP studies in rodents
  - GLP and non-GLP bioanalytical services
  - PK modeling
- **Biopharmaceutics Classification System (BCS)**
  - Permeability, solubility and dissolution
  - Regulatory filings for obtaining biowaivers

# Time Dependent Questions \*



No regulatory requirement to prove BE until after efficacy established

- Objective:  
Answer ? cost effectively
- Eliminate “unnecessary” *in vivo* BE
  - Most expensive way of ensuring performance
  - Unnecessarily exposures to healthy subjects
  - Can be less precise (Class I + high first pass)

# Value of BCS Assessments

## ➤ Discovery

- Series Characterization – Oral Delivery Potential
- Series Selection

## ➤ Lead Selection

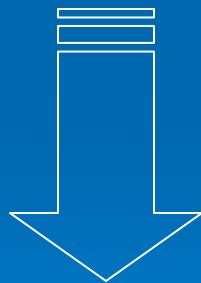
- Best candidate
- Delivery Strategy – formulation considerations

## ➤ Clinical Development

- NDA
  - Complement / strengthen mass-balance data
  - SUPAC – BA/BE biowaivers
- ANDA – BA/BE biowaivers

# Cost and Time Savings through BCS\*

- Bioequivalence Study Costs ~\$250,000
- **For BE studies that are rate limiting**
  - ~6 wk. between study start & results
  - Assuming peak sales \$1 billion/year



6 wks x \$1 billion/yr x 1 yr/52 wks

➤ **+\$110 million sales/study**

# Costs vs Savings \*

## ➤ Cost:

- Characterization: ~\$10,000 - \$60,000/drug
- Evaluation: ~\$15,000/formulation

## ➤ Savings:

- Save 50%+ cost of *in vivo* BE trials
- Potential drug development time savings

## ➤ Possible Strategies

- Fully characterize all compounds: Savings = Cost
- Characterize likely Class I (&III): Savings >> Cost

# Experimental Methods to Assess BCS Classes

- Human  $P_{\text{eff}}$
- *In situ* rat perfusion
- Human mass-balance
- Caco-2/MDCK

# Why TSRL as Partner for BCS?

- World experts in oral drug delivery
- Co-authors of regulatory guidance documents
- Dedicated service to pharmaceutical companies for over 20 years
  - GSK, Eli-Lilly, BMS, Nektar, Chiron, Gilead, RWJohnson, Searle and more...
- Integrated laboratory facilities for GLP and non-GLP contract work
- Expert consulting on oral delivery limitations

# Partnering Opportunities

- Contract research for BCS classification, oral absorption problem solving, and PK/ADME assessments
- Research collaborations and licensing agreements for delivery technologies