

*Emisphere*

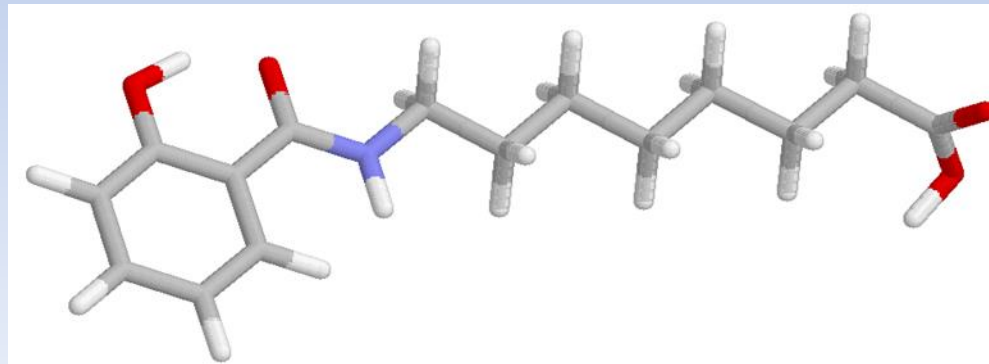
Eligen® Technology  
Summary and  
Value Proposition

# What Does Eligen® Technology Offer?

- **Eligen® Technology improves oral Bio-Availability**
  - Eligen® increases the rate and extent of absorption
  - Particularly relevant for large, injectable drugs
  - Peptides, proteins, oligosaccharides and oligonucleotides
  - Can enhance small molecule absorption as well
  - Can facilitate faster onset of action (eg, pain, nausea)
  
- **Characteristics of drugs that benefit from Eligen® Technology**
  - Molecular size
  - Deficient membrane partitioning profiles
  - Susceptibility to degradation

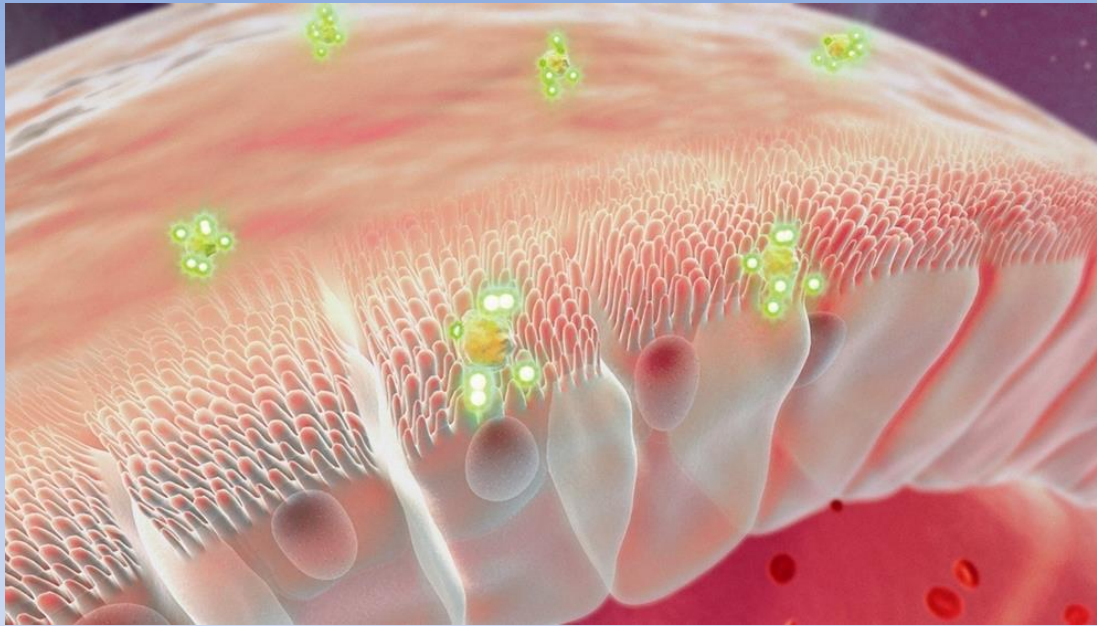
# Characteristics of Carriers

- Small molecules, stable and water soluble
- Affect membranes at low concentrations
- Weakly interact with the drugs that they deliver
- Solid (tablet or capsule) or solution/suspension are all viable options



SNAC

# Eligen® Technology - Mechanism of Action



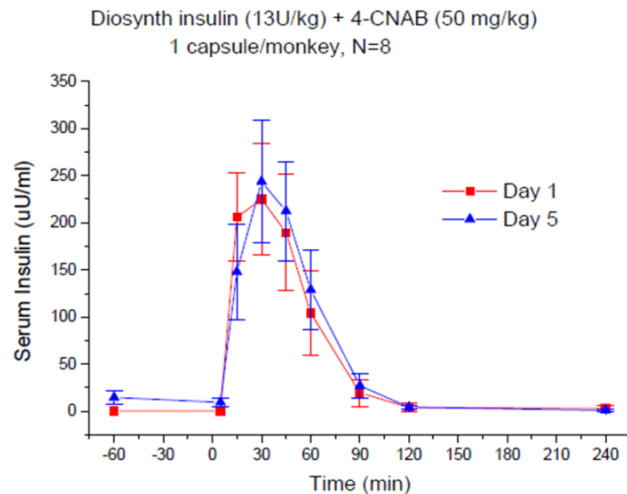
- Eligen® Technology binds a Delivery Agent with a Therapeutic Compound
  - Does not alter the Therapeutic Compound
  - Occurs when both Delivery Agent and compound are in close proximity
- Delivery agent chaperones compound through the gastrointestinal (GI) membrane

# Molecules Orally Delivered with Eligen® Technology

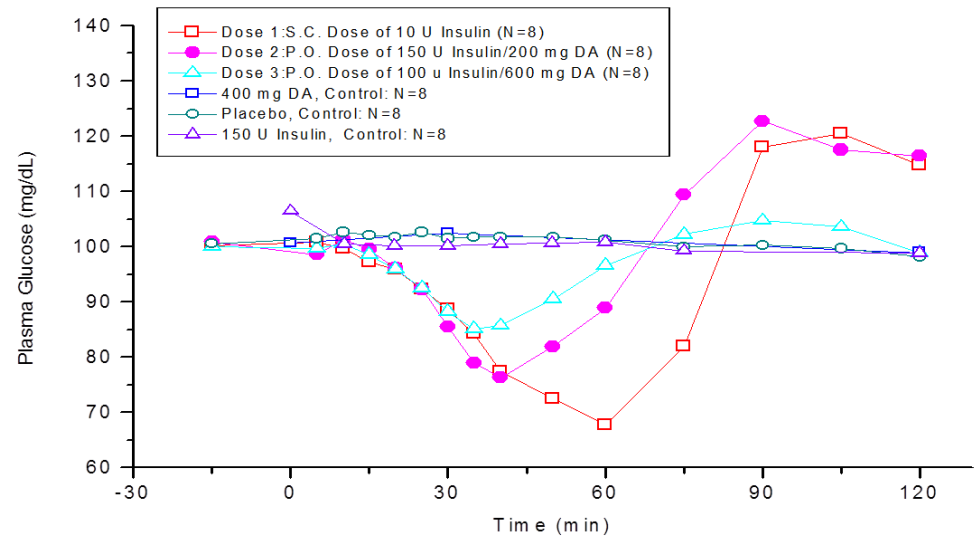
- **Peptides and Proteins**
  - Includes GLP-1, insulin, calcitonin, PTH, growth hormone, PYY
- **Small Molecules**
  - B12, ibandronate, cromolyn, triptans
- **Miscellaneous**
  - Heparin, low molecular weight heparin, gallium, oligonucleotides

# Proven Efficacy of Eligen® Technology

## 4-CNAB Allowed Absorption of Oral Insulin



## Absorbed Insulin Remains Active



PK / PD Study in Cynomolgous Monkeys  
- No absorption of insulin without 4-CNAB

In Man optimized dose:  
300U Insulin ±4-CNAB (160 mg)  
N= 6 or 7

# Strong Intellectual Property Position

- **Carrier Patents**

- Each carrier provides its own strong IP (NCE's)
- Ancillary patents may be achievable on polymorphs, salt forms, process of manufacture, etc.
- Applications filed widely in the US, Europe and throughout the world

- **Combination Patents**

- Combination patents on carrier and drug may provide extended protection

# Regulatory Considerations

- **Safety**
  - Several Eligen® carriers have toxicology data on file to support their use in Phase 2 and Phase 3 trials
  - One Eligen® carrier (SNAC) has been granted GRAS\* status for use with food supplements, vitamins and dietary ingredients
  - Several thousand human patients have received formulations containing Eligen® Technology carriers without the emergence of safety issues
- **Regulatory Strategies**
  - Eligen® Technology carriers can support 505 (b)2 submissions

\* GRAS substances do not require pre-market approval, subject to compliance with dose limits



# Emisphere Oral Carrier “Value Proposition” for Strategic Partnerships

- Carriers can convert specific safe/effective injectable therapeutics into oral formulations
- Technology with de-risked, approved APIs offers high probability for regulatory approval
- “Practical innovation” in portfolio strategy “hedges” ROI & complements “pure innovation”
- Carrier partnerships facilitates & sustainable product/franchise LCM strategies
- EMIS “wheel-house”: newer, smaller approved peptides & small molecules therapeutics
- Oral delivery critical in chronic-treatment TA’s such as: oncology, diabetes, autoimmune, etc.
- EMIS 30 years of expertise provides sponsor with rapid assessment of API/carrier match
- Low-cost/quick feasibility work quickly identifies/determines clinical success probability
- Complex healthcare economic/regulatory forces favor technology investment for ROI
- EMIS is a proven “center of excellence” for R&D firms to partner with on oral formulations
- Partnership Example: Novo Nordisk w/Phase 3 Oral GLP-1 & four new additional molecules

# Conclusions

- Eligen® Technology offers significant benefits to enhancing the absorption of orally administered products
- Emisphere owns significant IP around a large library of carriers
- Emisphere is working with multiple partners to facilitate oral delivery of a number of peptides
- Emisphere is interested in developing new relationships with new Partners to facilitate the development of orally administered drugs