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 Cynomologous 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