Introductions

• Located in Bethlehem, PA, ~50,000 sq ft integrated facility, 90+ employees
• Full service CDMO including commercial production and traditional CMC services
• Wide range of dosage forms, specialize in complexity
• 7,000+ sq. ft. of GMP production suites: sterile, non-sterile, and high potency
• FDA registered, DEA licensed
Agenda: Microparticles as Controlled Release Drug Delivery Systems

- What are microparticles?
- Why choose microparticles?
- Commercial microparticulate products
- Methods of preparation
- Preparation considerations
- Particle Sciences’ microparticle capabilities
What Are Microparticles?
Microparticle Drug Delivery Systems Can Align with Important Goals

- Controlled release from single injection-tunable duration of efficacy
- Biodegradable/biocompatible GRAS carrier materials
- Small molecules and biologics
- Range of loading capability
- Delivery of water soluble or insoluble products
Why Choose Microparticles?

- Protect unstable drugs
  - Before and after administration
- Provide accurate delivery of small quantities of potent drugs
- Provide ability to manipulate:
  - pK profile
  - Cellular and tissue interactions
  - *In vivo* action of drugs
- Enable controlled release
Microparticle Advantages

- Improved Safety
- Improved Patient Compliance
- Improved Efficacy
- Why MPs?
- Improved Outcomes
- Cost Reduction
- Life Cycle Management

Sustained and Controlled delivery of an active over long periods of time
Microparticle Advantages

- Effective delivery of insoluble actives
- Bolus delivery instead slower IV administration
- Targeted drug delivery to specific sites
- Reduction of dose frequency and toxicity
- Ability to maintain drug in amorphous form
- Reduction of local side effects
- Maintenance of therapeutic plasma concentrations
### Examples of FDA-Approved Microparticulate Products

<table>
<thead>
<tr>
<th>Product Name</th>
<th>Active Ingredient</th>
<th>Route of Administration</th>
<th>Approval Date</th>
<th>Indication</th>
<th>Dosing Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Vivitrol® by Alkermes</strong></td>
<td>Naltrexone</td>
<td>Intramuscular</td>
<td>1984</td>
<td>Indicated for the treatment of alcohol/opioid dependence</td>
<td>Every 4 weeks</td>
</tr>
<tr>
<td><strong>Sandostatin® LAR Depot by Novartis</strong></td>
<td>Octreotide</td>
<td>Subcutaneous</td>
<td>1998</td>
<td>Indicated for treatment of acromegaly, severe diarrhea/flushing episodes associated with metastatic carcinoid tumors and VIP-secreting tumors</td>
<td>Every 4 weeks</td>
</tr>
<tr>
<td><strong>Arestin® by OraPharma</strong></td>
<td>Minocycline HCl</td>
<td>Periodontal</td>
<td>2001</td>
<td>Indicated as an adjunct to scaling and root planing (SRP) procedures for reduction of pocket depth in patients with adult periodontitis</td>
<td>Variable</td>
</tr>
<tr>
<td><strong>Risperdal Consta® by Janssen</strong></td>
<td>Risperidone</td>
<td>Intramuscular</td>
<td>2003</td>
<td>Indicated for the treatment of schizophrenia and bipolar I disorder</td>
<td>Every 2 weeks</td>
</tr>
<tr>
<td><strong>Lupron Depotstin® by AbbVie</strong></td>
<td>Leuprolide acetate</td>
<td>Intramuscular</td>
<td>1989</td>
<td>Multiple indications including prostate cancer, central precocious puberty, fibroids and endometriosis</td>
<td>Every 1, 3 or 6 months</td>
</tr>
</tbody>
</table>
Methods of Preparation

Preparation of Microparticles via Emulsion

1. Distilled Water Emulsifiers
2. Drug + Polymer + Solvent
3. Stirring
4. O/W Emulsion
5. Solvent Evaporation or Extraction
6. Microparticle Suspension Ready for Additional Processing

Spray Drying

1. Feed
2. Gas (in)
3. Drying Chamber
4. Cyclone
5. Gas (out)
6. Powder Product
Methods of Preparation

Jet Milling

Augmented Drip Casting

Grinding Chamber

Micronized Product Outlet

Feeder

Compressed Grind Air or Gas

Shell

Core
Preparation Considerations

Water Insoluble API

Water Soluble API

Liquid / Solution Encapsulation

Solid Encapsulation

Water Immiscible Solvent

Emulsion-Solvent Evaporation
Emulsion-Solvent Extraction
Spray Drying

Water Miscible Solvent

Coacervation/Phase Separation
Spray Drying

Washing
Filtration
Drying/Lyophilization
Sterilization
Resuspension for Dosing
Over 20 microparticle formulations in development at PSI over past 18 months from R&D through clinical production
PSI Processing Capabilities
When it comes to microparticulate formulations, Particle Sciences has the:

**Equipment**
- Fully equipped for development services and moving into commercial-scale equipment

**Facilities**
- 7,000+ sq. ft. of GMP production suites to accommodate 1 - 2 kg commercial batches

**Personnel**
- Decades of cumulative experience formulating and manufacturing microparticulate formulations
Concept to Commercialization

We Deliver®