

## MannKind Corporation

### Technosphere® Technology

#### Versatile Drug Delivery Platform

MannKind Corporation has developed the **TECHNOSPHERE® TECHNOLOGY PLATFORM**, a versatile delivery system that mimics the pharmacokinetics of intra-arterial administration.

#### Technosphere® Technology

**T**echnosphere® technology is a versatile drug delivery platform that allows the pulmonary administration of therapeutics currently requiring administration by injection. Technosphere technology offers several competitive advantages over other pulmonary drug delivery systems. Most notably, the pharmacokinetic profiles of drugs inhaled as Technosphere formulations are characterized by very rapid systemic absorption into the arterial circulation. In addition to rapid arterial delivery, drugs administered as Technosphere formulations avoid both hepatic first pass metabolism and degradation in peripheral circulation. Technosphere technology also offers the ability to conduct vehicle-controlled studies by inhalation of “blank” Technosphere particles.

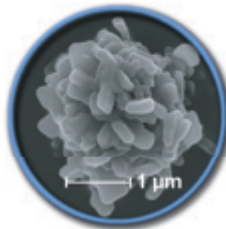
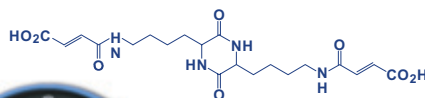
**T**echnosphere formulations have been prepared with a diverse assortment of drugs that have a broad range of physicochemical characteristics. For example, drugs ranging in molecular weight from 500 to 140,000 Da have been successfully adsorbed onto Technosphere particles. Anionic and cationic drugs, hydrophobic and hydrophilic drugs, proteins, peptides, and small molecules have all been formulated successfully. Systemic drug delivery using many of these formulations has been demonstrated in a rat model of pulmonary drug delivery. Clinical drug delivery has been demonstrated with insulin/Technosphere, PTH/Technosphere, sCT/Technosphere, and GLP-1/Technosphere.

#### Technosphere® Inhalation System



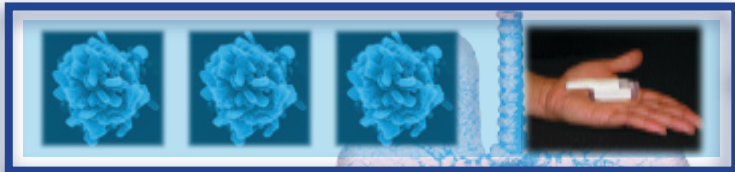
#### Technosphere® Technology

Technosphere® microparticles are formed by the acid-induced self-assembly of FDKP (fumaryl diketopiperazine) molecules



*Crystalline plate assembly*  
*Extremely high surface area*

Technosphere technology is based on the pH-induced intermolecular self-assembly of a novel small molecule excipient (FDKP) to form microparticles, called Technosphere® particles



MannKind Corporation

## Technosphere® Technology Versatile Drug Delivery Platform

### Technosphere® Technology (continued)

Technosphere technology enables the delivery of a variety of different drugs through the design and preparation of novel particles. Thus, MannKind's particle formation and formulation expertise is being expanded to include a number of particles with the potential to meet an assortment of drug delivery challenges.

While the technology is currently focused on pulmonary drug delivery for systemic absorption, research studies indicate the Technosphere platform has potential applicability for local lung delivery as well as other routes of administration. Technosphere technology has the potential to provide impressive drug delivery solutions across a wide variety of therapeutic areas encompassing a number of diverse products and disease states.

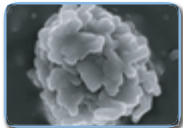
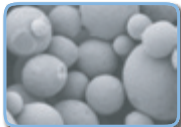
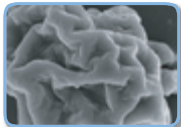
### Advantages

The unique pharmacokinetic profiles of drugs inhaled as Technosphere formulations have the potential to provide significant competitive advantages over drugs delivered via other delivery systems, including:

- Applicability to a wide variety of drugs
- Rapid drug absorption that mimics intra-arterial delivery
- Excellent bioavailability
- Improved convenience with patient-friendly, needle-free devices

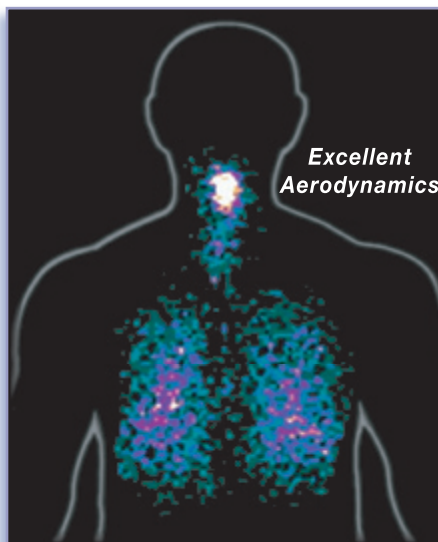
### Technosphere® Formulations

Range of API Physicochemical Characteristics  
Appropriate for Technosphere® Technology

Input	Output
Proteins, peptides, mAbs, vaccines, small molecules	 <i>Technosphere® Insulin</i>
Anionic, cationic	 
Hydrophobic, hydrophilic	

Technosphere® formulations have been prepared with a diverse assortment of drugs

### <sup>99m</sup>Tc-labeled AFREZZA®



<sup>99m</sup>Tc-labeled AFREZZA® demonstrates uniform distribution to the deep lung

For more information about MannKind Corporation and its technology, visit: <http://www.mannkindcorp.com>

