Silica-Based Nanoparticles as Therapeutics for Osteoporosis

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December 13, 2011

Gateway to Discovery, Innovation, and Products
By The Numbers...

50 – percent of women over 50 who will suffer osteoporosis-related fracture

25 – percent of men over 50 who will suffer osteoporosis-related fracture

24 – percent of hip fracture patients over 50 that die in the year following their fracture

34 million – Americans with low bone mass

10 million – Americans with osteoporosis

Data Courtesy of National Osteoporosis Foundation
The Bone Cycle

OSTEOBLAST: Bone building cells
OSTEOCLAST: Bone resorbing cells

FORMATION
RESORPTION
Bone Growth

Bone Modeling - growth and sculpting to achieve optimal size and load bearing capacity

There is a net gain of bone mass
Bone Resorption

Bone Formation

AGE

Bone Resorption
Bone Resorption

Bone Formation

Bone Resorption

AGE
Homeostasis

No net gain or loss of bone mass

Remodeling replaces 10% of the skeleton/year
Bone Resorption

Bone Formation

Bone Resorption

AGE
Osteoporosis

An imbalance between formation and resorption

There is a net loss of bone mass
Osteoporosis in Pictures

Healthy Bone

- Loss of BMD
- Loss of Structural Integrity

Osteoporotic

- Loss of Load Bearing Capacity
- Increased Propensity to Fracture

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# Current Therapeutics

<table>
<thead>
<tr>
<th>Name</th>
<th>MOA</th>
<th>Disadvantages / Side Effects</th>
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| Fosamax®         | Anti-resorptive; inhibits bone breakdown | Suppresses bone formation  
                   |                                                                 | Bone is not remodeled correctly  
                   |                                                                 | Severe GI side effects  
                   |                                                                 | Increased risk of some fractures  
                   |                                                                 | Certain genders excluded |
| Boniva®          |                                 |                                                                   |
| Actonel®         |                                 |                                                                   |
| Reclast®         |                                 |                                                                   |
| Calcitonin       |                                 |                                                                   |
| Evista®          |                                 |                                                                   |
| Forteo®          | Pro-osteoblastic; promotes bone growth | Requires daily injection  
                   |                                                                 | Associated with osteosarcoma  
                   |                                                                 | Can only be taken for 1 year  
                   |                                                                 | Incompatible with anti-resorptives |
I SMELL OPPORTUNITY

“An ideal way to prevent age-related bone loss would be not only to reduce bone resorption, but also to promote bone formation.”

Dr. Pierre Marie, Medicographia. 2010;32:10-17
Solution = Silica Nanoparticles

- Nanoparticles have different properties compared to bulk particles
- Eating sand will not cure osteoporosis!!!!!! Nanoscale is critical!
Silica Nanoparticles Inhibit Osteoclast Formation

Graph showing the effect of RANKL and NP1 on osteoclast formation and cell viability in RAW 264.7 cells. The graph indicates that increasing concentrations of NP1 reduce both osteoclast formation and cell viability.
Silica Nanoparticles Promote Osteoblast Formation
Mouse Data

Young Mouse

- NP1-MNP-PEG
- Vehicle

Old Mouse

- Vehicle
- NP1-MNP-PEG

Femoral BMD (% Change from Baseline)

Time (weeks)

BMD (mg/cm²)

Time (Weeks)

BV

BV [mm³]

Vehicle

NP1-MNP-PEG
Intellectual Property

- US and European Patent application pending
  - covers method of treating osteoporosis and other degenerative bone disorders using silica nanoparticles

- Emory has filed provisional patent claiming composition of riboflavin-doped silica nanoparticle
Drug Development

- Measuring Therapeutic Index, assessing toxicity, and estimating pharmacokinetics
- Assessing difference modes of delivery (oral, inhalation, IV, etc.)
- Quantifying relative contributions of size, shape, charge, and composition of silica nanoparticles
- Drug development work being led by James Sikorski, Ph.D., and being funded by GRA