



**Pioneering** the next generation  
of drug delivery and biosensing

Unither Nanomedical  
and Telemedical  
Technology Conference  
April 3, 2008

James Prescott



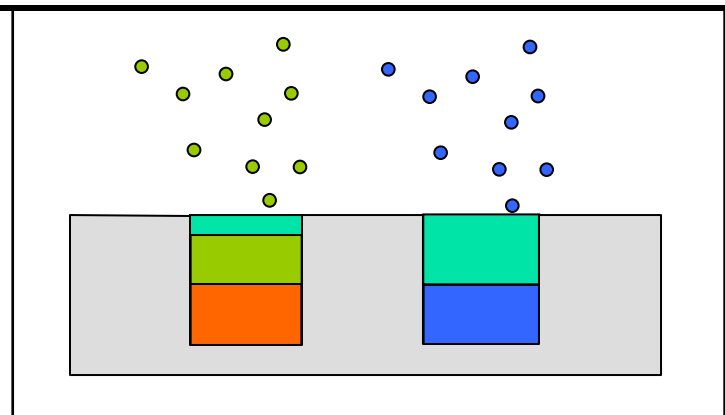
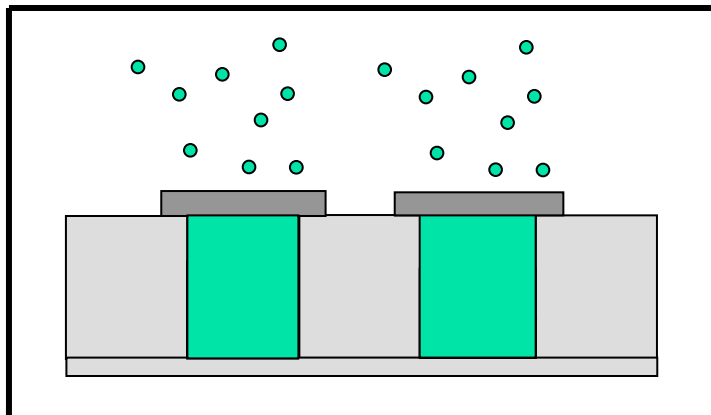
MicroCHIPS, Inc. is creating sophisticated implanted devices to provide drug delivery and monitoring for chronic and debilitating medical conditions.

## MicroCHIPS Reservoir Technology

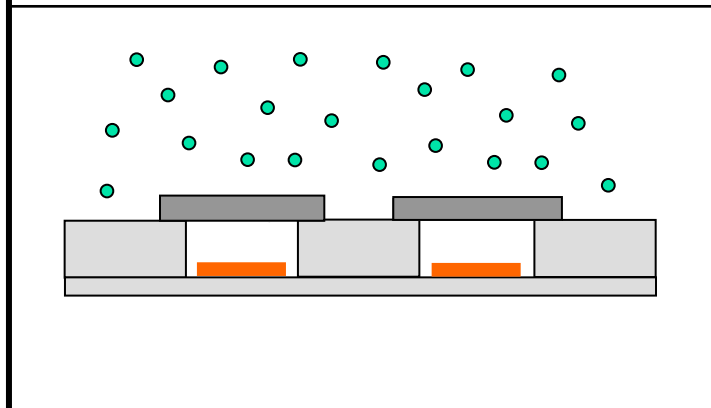
Active

Passive

Drug  
Delivery



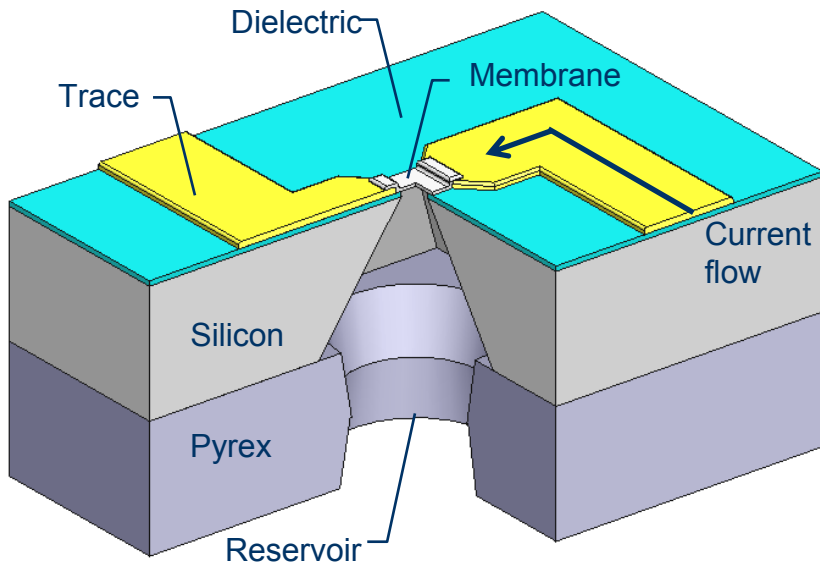
Biosensing



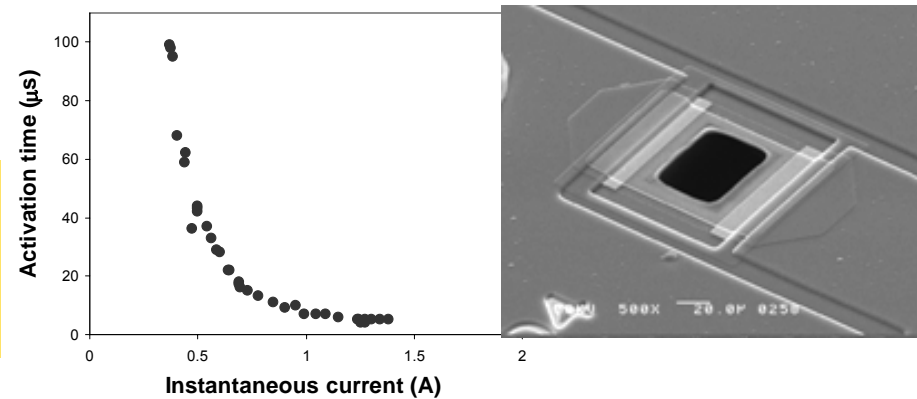
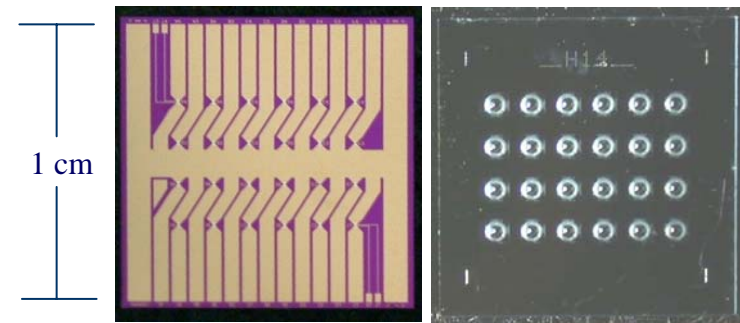
Focus on (but not limited to)  
implantable devices

MEMS and non-MEMS technology

## Active Controlled Exposure Technology



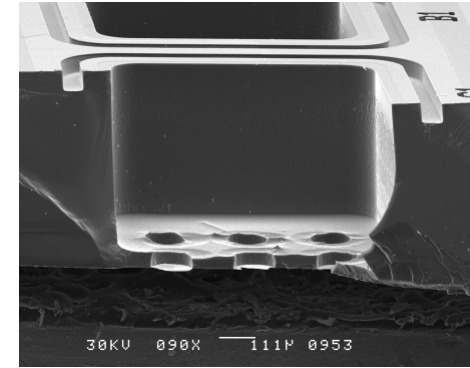
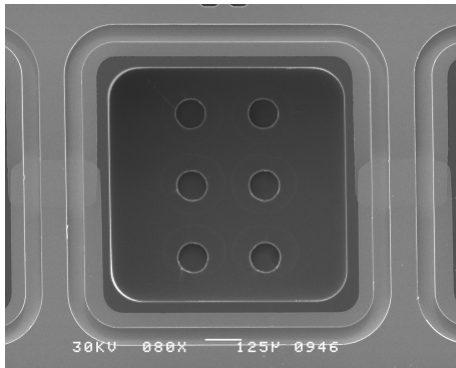
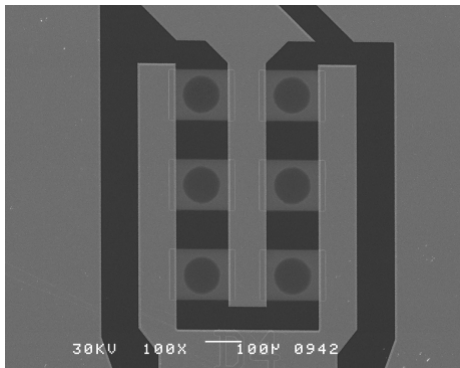
3800Å Pt-Ti-Pt membrane is extremely robust...withstands static pressures >400 psi, fatigue testing ~100,000,000 cycles from 20-45 psi in saline at 37°C with no failures



## Multi-reservoir, microchip based arrays

Versatility of MEMS processing provides performance optimization via array design. A prototype multi-reservoir array fabricated with an anisotropic etching technique is shown below. This design provides:

- larger volume
- larger reservoir exposure areas on activation
- hermetic sealing of individual reservoirs.



(Scale: Reservoir “footprint” of  $800\mu\text{m} \times 800\mu\text{m}$ , Array thickness  $525\mu\text{m}$ )



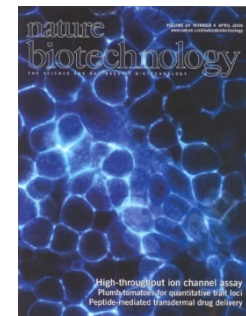
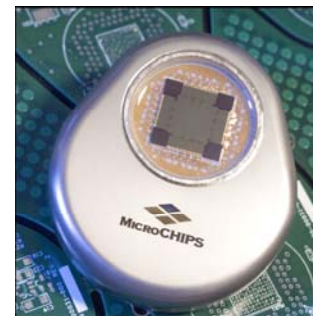
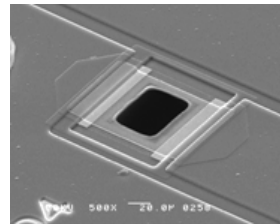
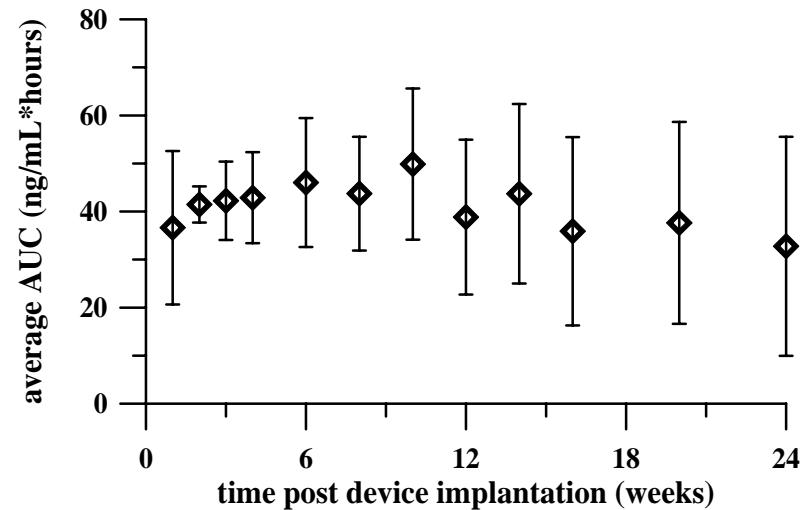
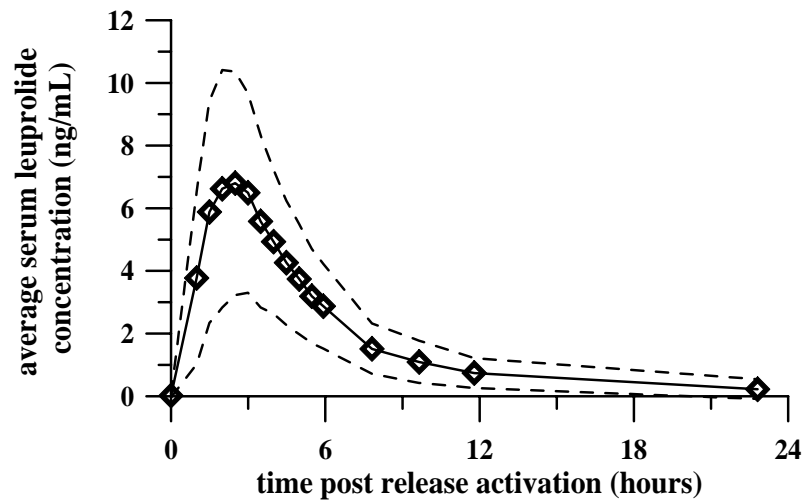
# Drug Delivery Platform

# **Active Implants for On-Demand Delivery**

## **Drug Delivery Platform**

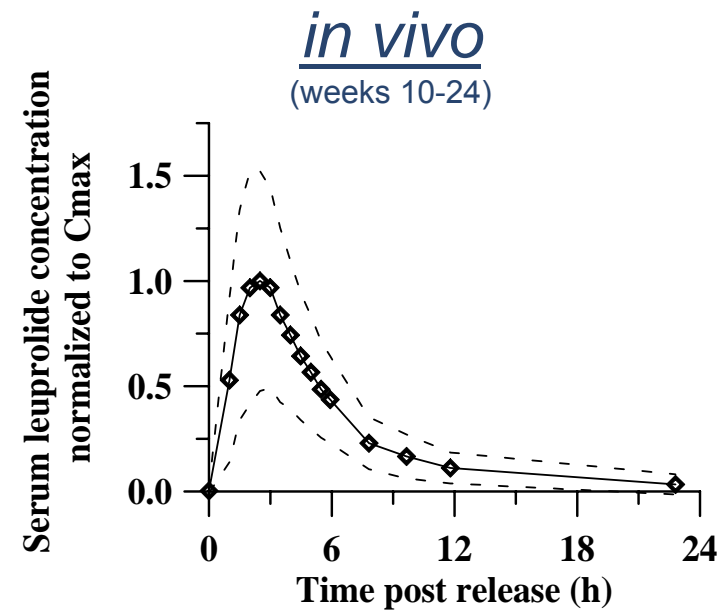
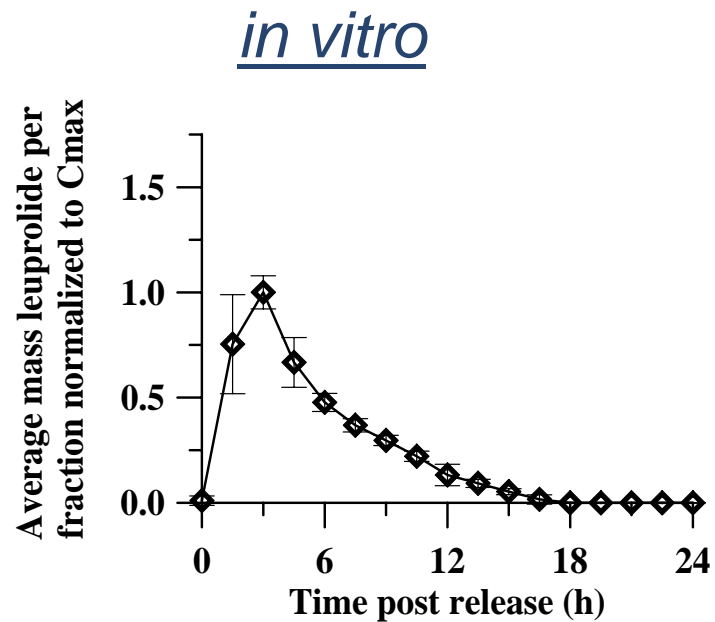
## Leuprolide – *in vivo* PK & Bioavailability

Pulsatile release demonstrated for 6 months



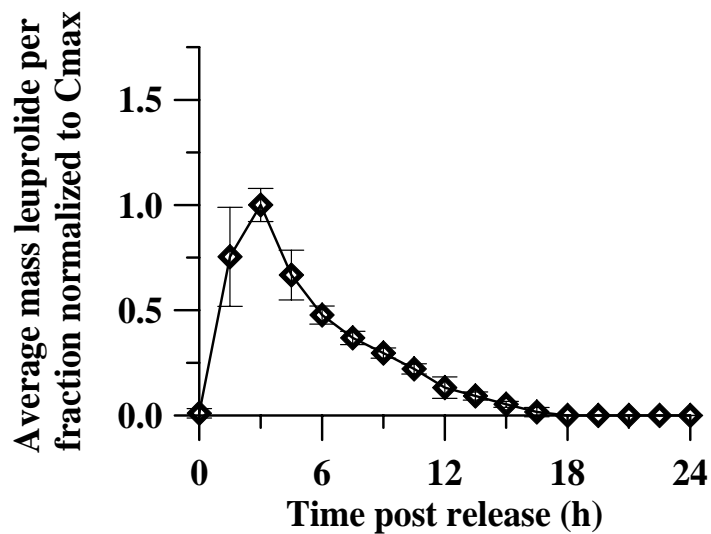
Prescott *et al.*, *Nature Biotechnology*, **24**, 437-438 (2006).

## Leuprolide – *in vitro* Kinetics vs. *in vivo* Pharmacokinetics

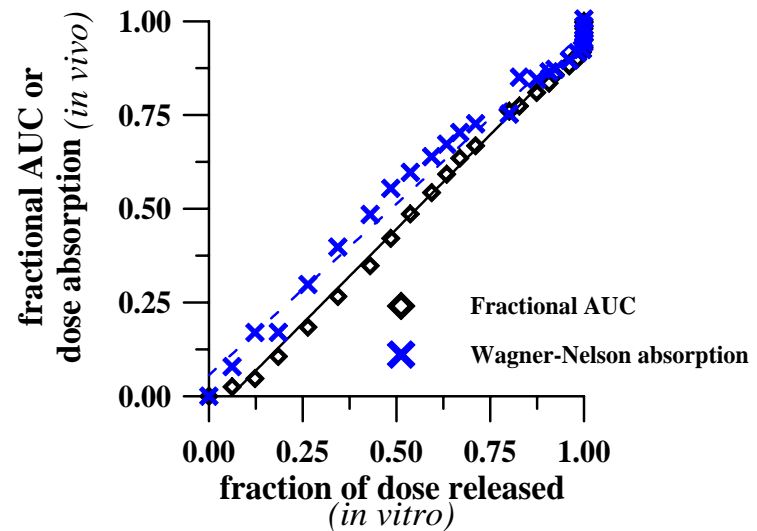


# Leuprolide – *in vitro* Kinetics vs. *in vivo* Pharmacokinetics

## *in vitro* release kinetics

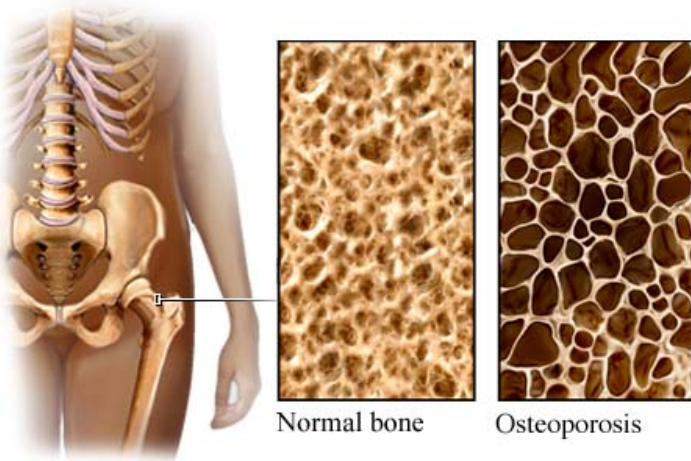
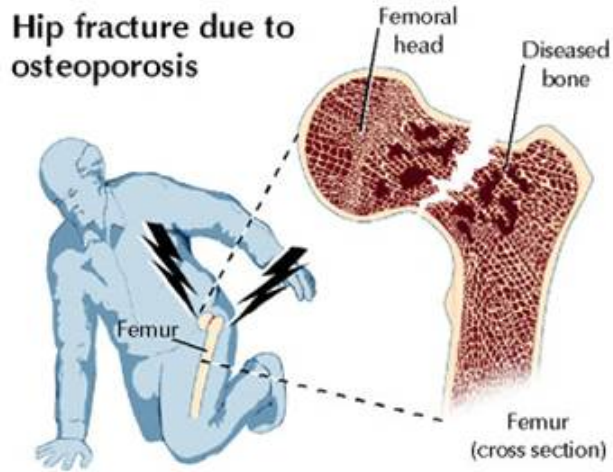


## *in vitro* – *in vivo* correlation

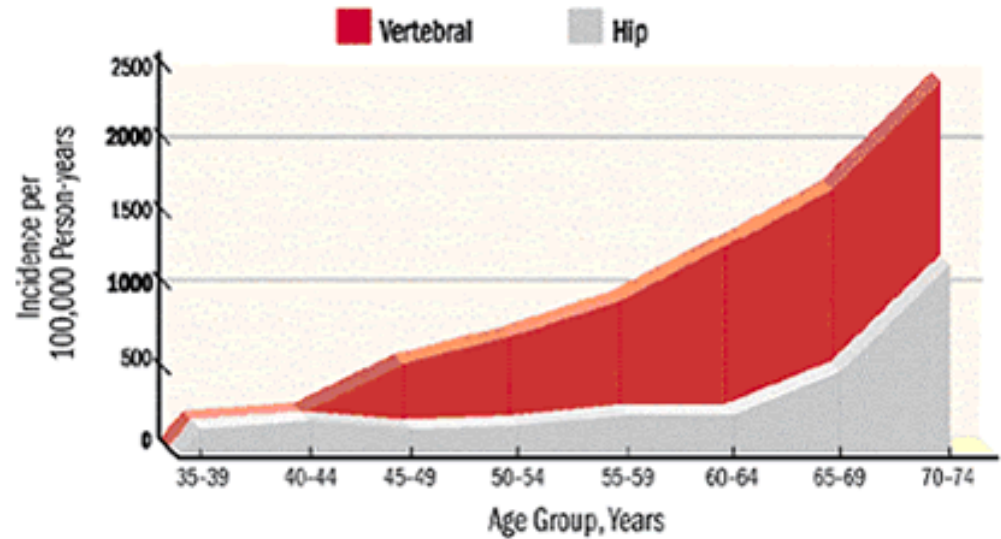


# Osteoporosis – The Silent Killer

Hip fracture due to osteoporosis



Incidence of Fracture Among Women



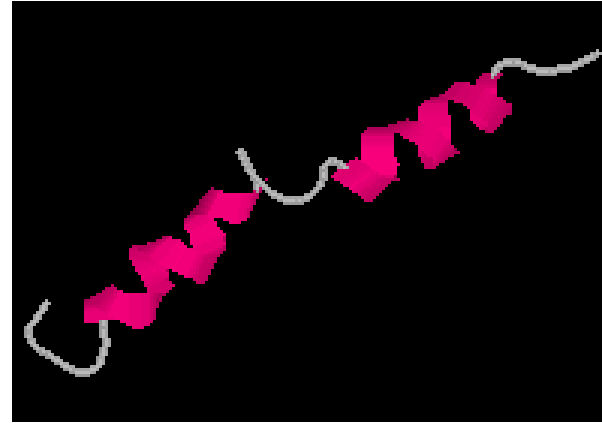
Direct annual cost of osteoporotic hip fractures: \$18 billion in 2002

-- National Osteoporosis Foundation

US Market: 10M Osteoporosis  
34M Osteopenia

**H-1Ser-Val-Ser-Glu-5Ile-Gln-Leu-Met-His-10Asn-Leu-Gly-Lys-His-15Leu-Asn-Ser-Met-  
Glu-20Arg-Val-Glu-Trp-Leu-25Arg-Lys-Lys-Leu-Gln-30Asp-Val-His-Asn-Phe-OH**

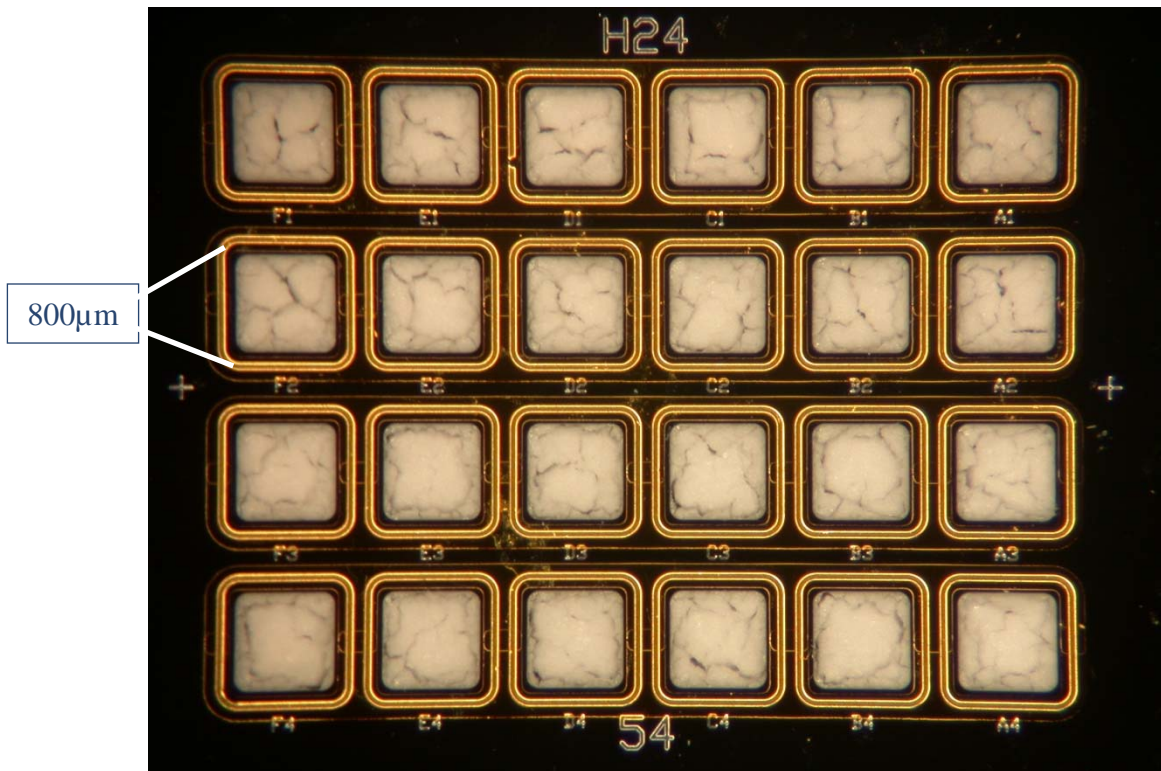
**Human parathyroid hormone (1-34), N-terminus**



(from U.C. Marx, University of Bayreuth, Germany)

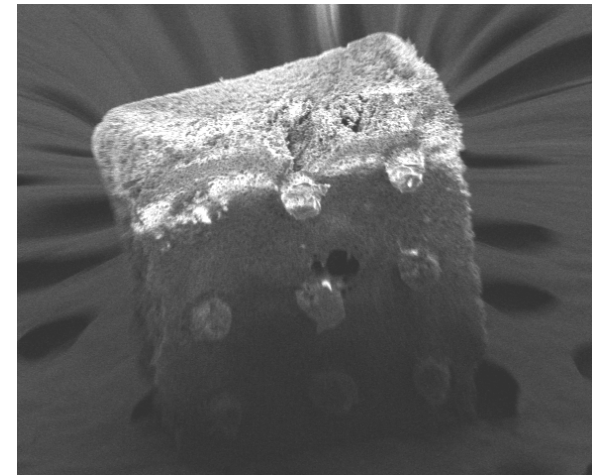
- Forteo™ (Lilly) daily administration of hPTH(1-34) by SC injection (20 µg peptide)
  - Promotes bone growth (increase in bone density)
  - Plasma PK: C<sub>max</sub> in 30 minutes, return to baseline levels within 4 hours
- hPTH(1-34) administered with zero-order release kinetics favors bone resorption – catabolic effect.

## hPTH (1-34) lyophilized in a micro-reservoir array

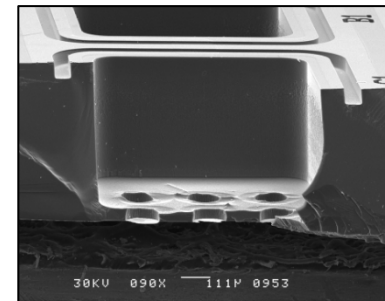


- 24 discrete dosage forms (20 µg per reservoir)
- Starting solution concentration  $\geq 100\text{mg/mL}$  hPTH (1-34)
- Array dimensions 10mm x 10mm x 0.525mm (thickness)

Scanning electron micrographs



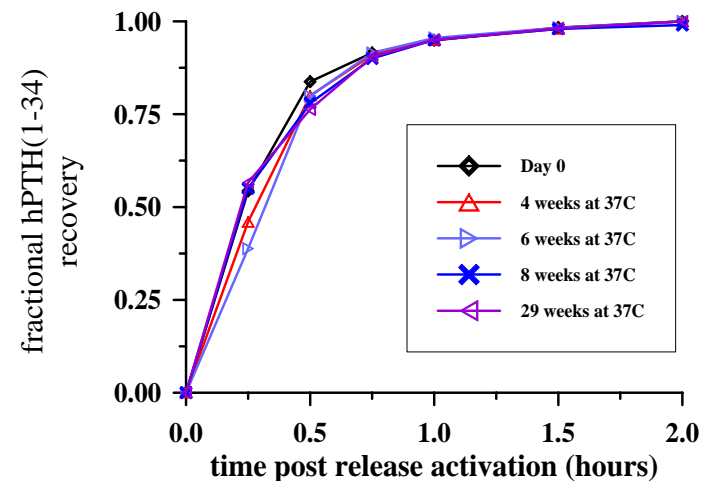
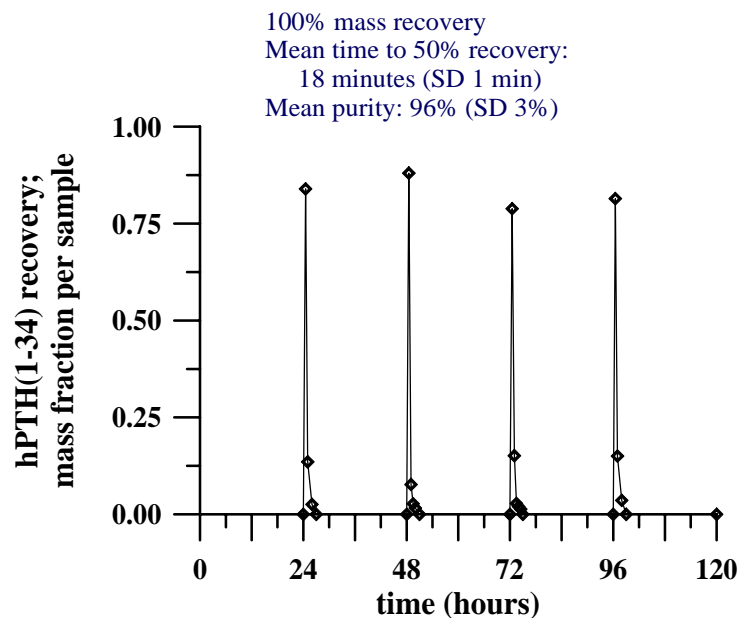
**Lyophilized hPTH (1-34) dosage form**



**Cross section of reservoir interior**

## hPTH (1-34) *in vitro* Results

Pulsatile release – rapidly dissolving lyophilizate of hPTH (1-34)



Purity at 37°C:

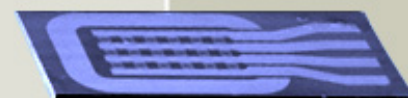
- 8 weeks, 95% (CV 2%)
- 12 weeks, 94% (CV 3%)
- 24 weeks, 86% (CV 3%)

## hPTH (1-34) *in vivo* Studies

- Pharmacokinetic (PK) study to demonstrate release of PTH in subcutaneous implant
  - Canine model
  - Comparison to subcutaneous injection
  - Bioavailability
  - Changes in PK over time
- Efficacy study
  - Ovariectomized rat model
  - Comparison to subcutaneous injection and no treatment (control groups)
  - Monitor increase in bone mineral density (BMD)



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