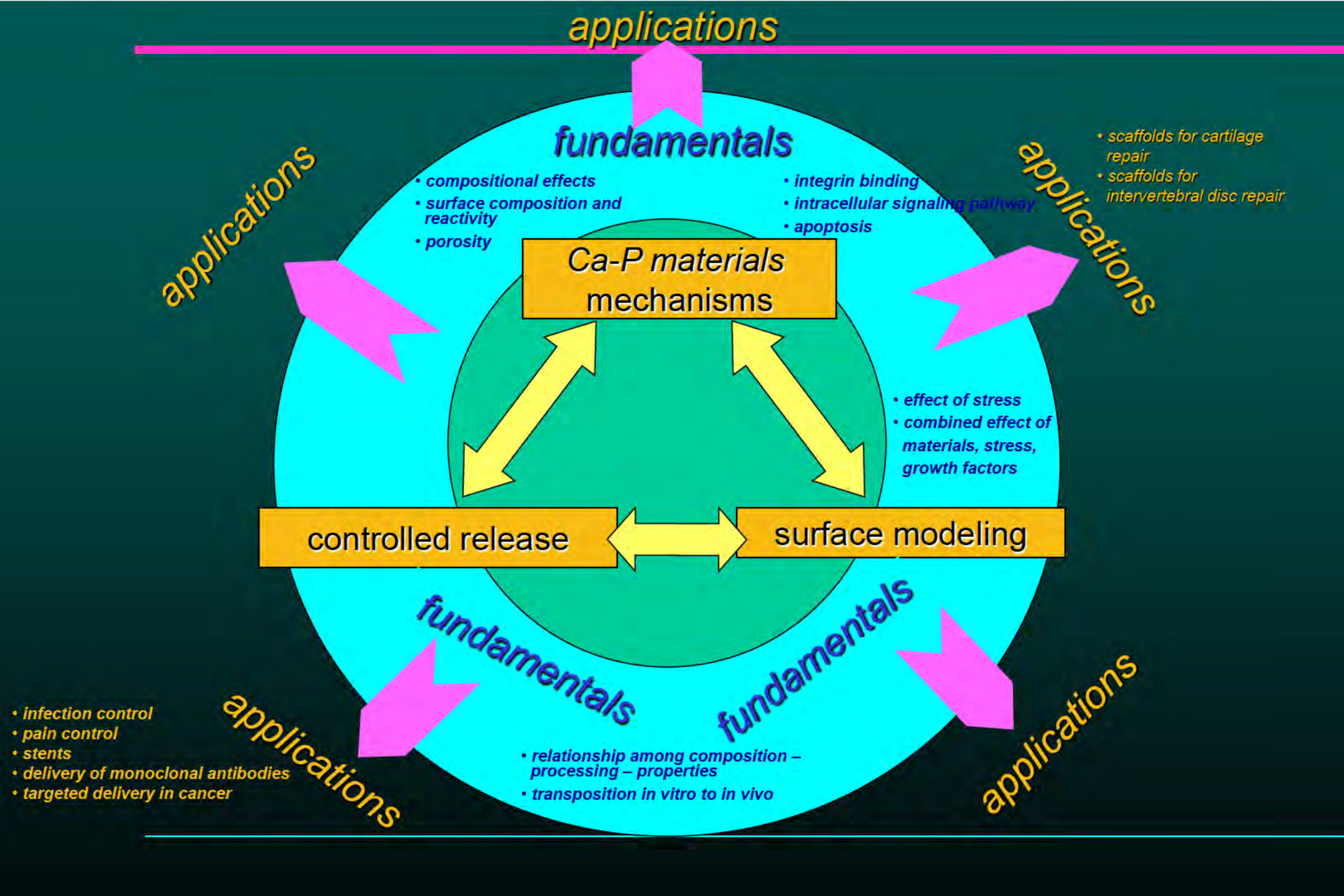
Orthovita to Gentis to XeroThera

Spin-outs from Penn

Concepts at the origin

Paul Ducheyne

University of Pennsylvania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• porosity
• integrin binding
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• scaffolds for cartilage repair
• scaffolds for intervertebral disc repair
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Ca-P materials
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• effect of stress
• combined effect of materials, stress, growth factors
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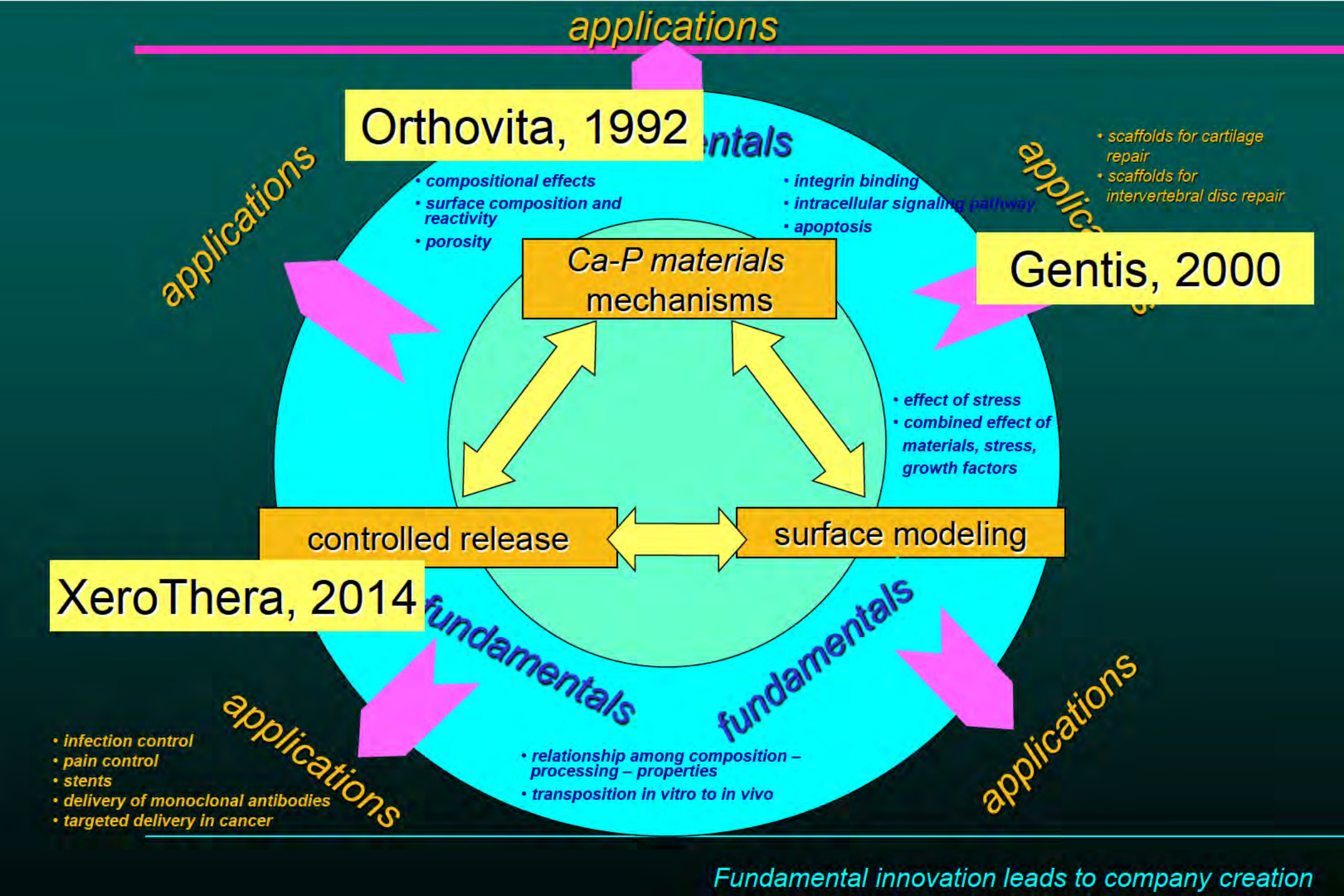
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Fundamental innovation leads to company creation

Collaboration Academia - Industry Educational Value

- **Engineering: the application of laws of physics and chemistry, and the knowledge from biology to the benefit of society.**
  Our teaching gains in depth by first hand insight into the organizations that apply this knowledge.

- **Role models in education:**
  With applicability being central to the engineering profession, the guidance by educators towards implementation of concepts makes for very powerful examples in engineering education.

Collaboration Academia - Industry Educational Value

- Ph.D thesis work is very focused, and typically does not span the whole spectrum from fundamental to applied work:
  However, if the lab covers the range from the fundamental to the applied, Ph.D. trainees are exposed to the very broad nature of engineering science.

Collaboration Academia - Industry Biomaterials Needs

- Statistically valid analyses of the interaction between materials and living tissues require large sample populations:
  University laboratories typically do not have the facilities, nor the mentality for making large series of samples reproducibly.

Collaboration Academia - Industry Biomaterials Needs

- **The ultimate goal of biomaterials research is to improve clinical outcomes:**
  One cannot document clinical benefits without clinical studies. Academia is not well organized to conduct biomaterials related clinical studies by itself.

Collaboration Academia - Industry Specific relationships

- Industry sponsored research in academia
  - » Contract, proprietary research
  - » Consortium research
  - » Clinical studies
- Off campus interactions
  - » Sounding board function in strategic planning
  - » Product development support
  - » Production issues
  - » Regulatory aspects
  - » Technical legal matters, such as those related to intellectual property and product defense

Collaboration Academia - Industry Specific relationships

- Technology transfer and license agreements
  - » with existing concerns
  - » by creating a new corporation (“start-up”)

Collaboration Academia - Industry Creation of a start-up

- Fundamentally new technology for which an appropriate industrial organization does not exist. By forming a new corporate entity, technology is advanced, employment is created and society's wealth is enhanced.

A biomaterials company

Orthovita, a biomaterials company
A broad materials platform

- Source 1: European advanced materials concern (F.B.F.C. International, Inc.)
- Source 2: University of Pennsylvania
- Source 3: Orthovita's own R & D

ORTHOVITA

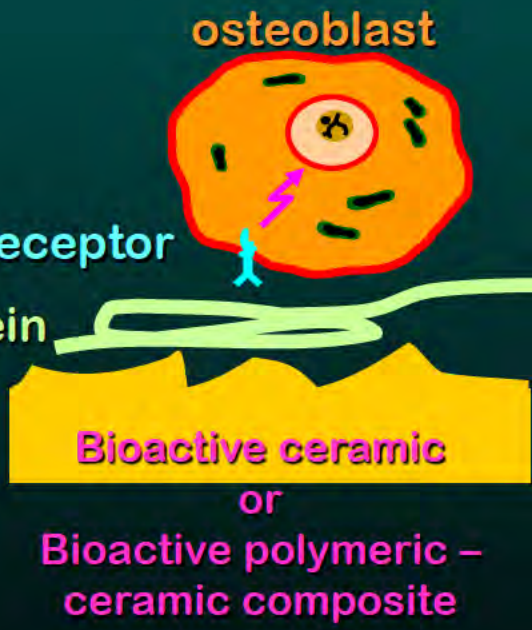
Orthovita,
A biomaterials *company*

- Educational institutions and corporate organizations have different overall objectives
  - » Academia: knowledge creation and dissemination
  - » Industry: engine of society's wealth creation
- Relational cliffhangers
  - » The company exists as the funding vehicle of the university lab
  - » The university lab is the extension of corporate R & D
- ***An arm's length relationship is essential for both parties***

Orthovita (NASDAQ: VITA) – University of Pennsylvania A symbiotic relationship

- **U Penn's Center for Bioactive Materials and Tissue Engineering:**
  - » Fundamental analyses of material - tissue interactions of non-proprietary materials
  - » Diligent publication commensurate with the goal of dissemination of knowledge

- **Orthovita, a biomaterials company Opportunity and philosophy**
  - » a broad materials technology platform useful in devising bone substitutes and bone grafts that enable to match a wide range of patient needs

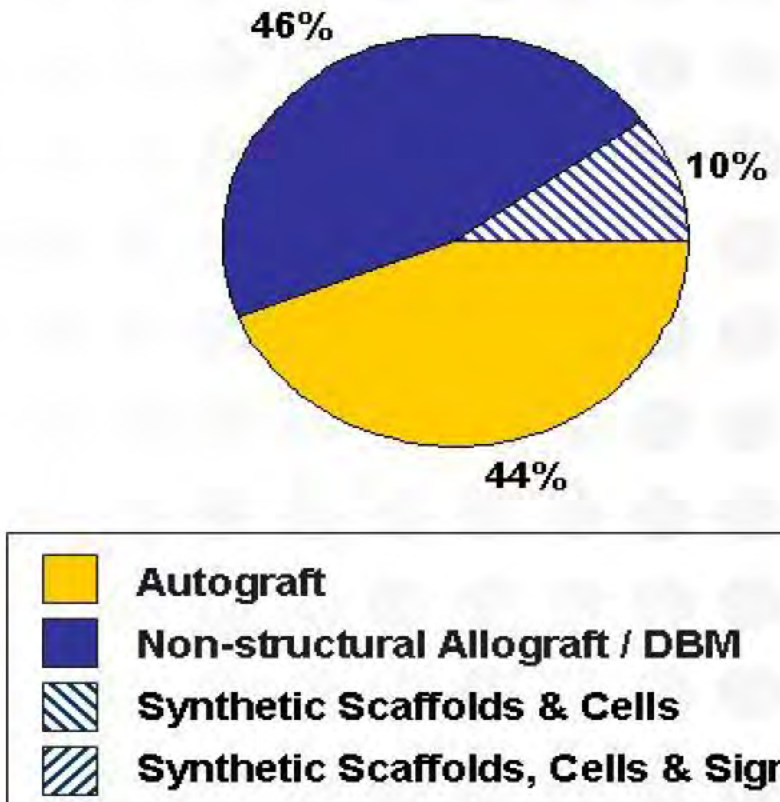


Orthovita's product platforms ca 2008

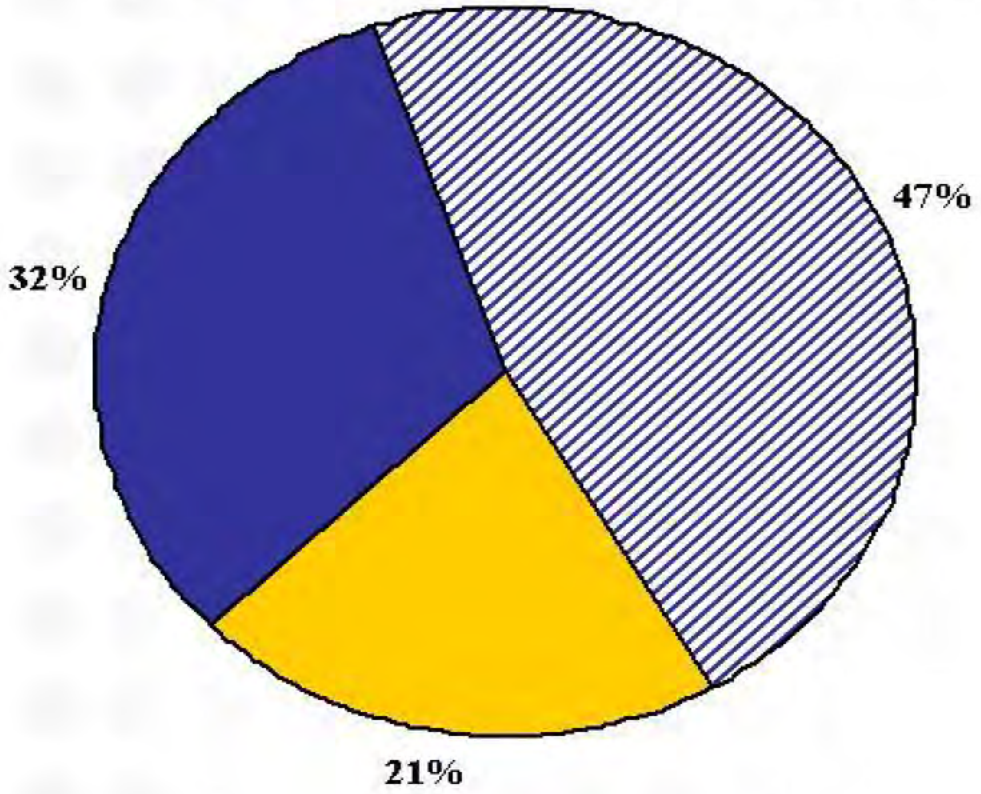
- Vitoss™: porous, nanostructured calcium phosphates
- Orthocomp™: high strength, bioactive composites
- Vitagel™: acquired from Angiotech

Non-Structural Bone Graft U.S.
Market Overview

2001 $360 MM Market

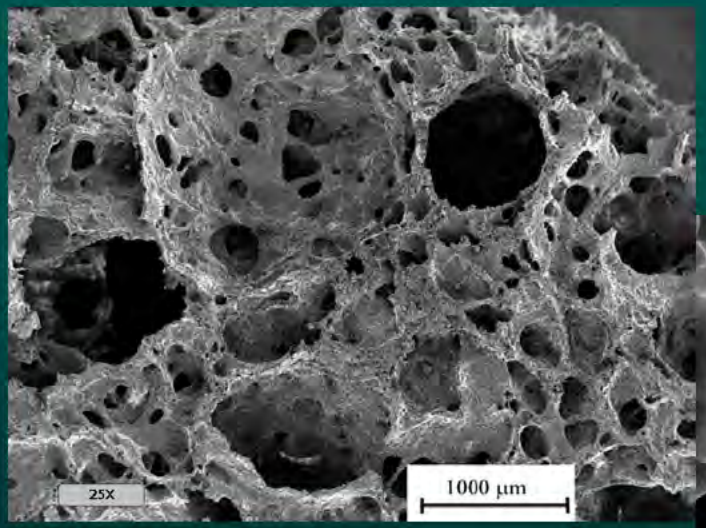


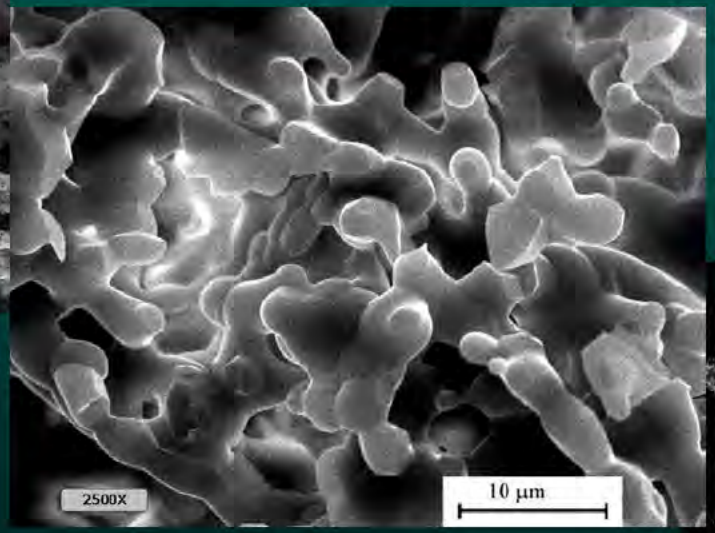
2007 $1,000 MM Market

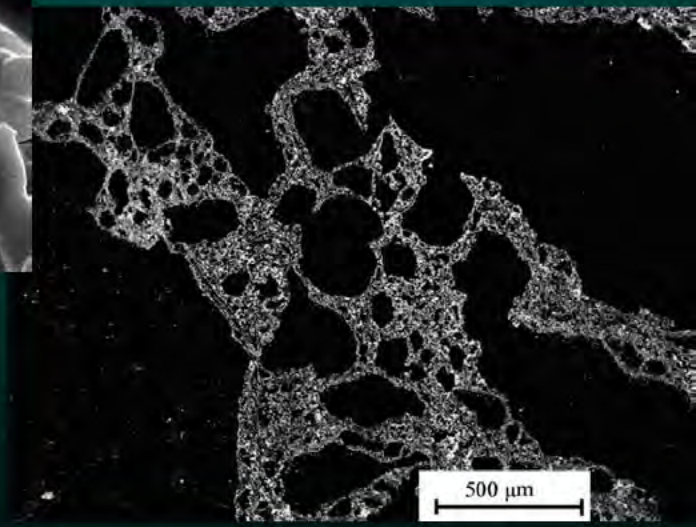


Source: Data Monitor; Market Dynamics: Bone Substitutes and Growth Factors, December 2002

Synthetic bone graft – Vitoss*







- surface reactivity
  - composition
  - specific surface area
- porosity

** 35 % market share, USA – synthetic bone grafts*

Orthovita's development

- Operations began in 1993
- EASDAQ Initial Public Offering, June 1998
- NASDAQ listed, from 2000
- About 270 employees
- Largest independent, dedicated biomaterials company in the world
- Acquired by Stryker in 2011

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XeroThera

Fifteen years worth of fundamental research

Silica xerogels (Silica sol-gels)

Room-temperature process

- Highly porous materials – porosity at the nanoscale
- Release properties controlled by the nanostructure

Sol-gel processing steps

Hydrolysis

$\equiv$Si-OR + H_2O $\rightleftharpoons$ $\equiv$Si-OH + ROH

Si-OR: Organosilane

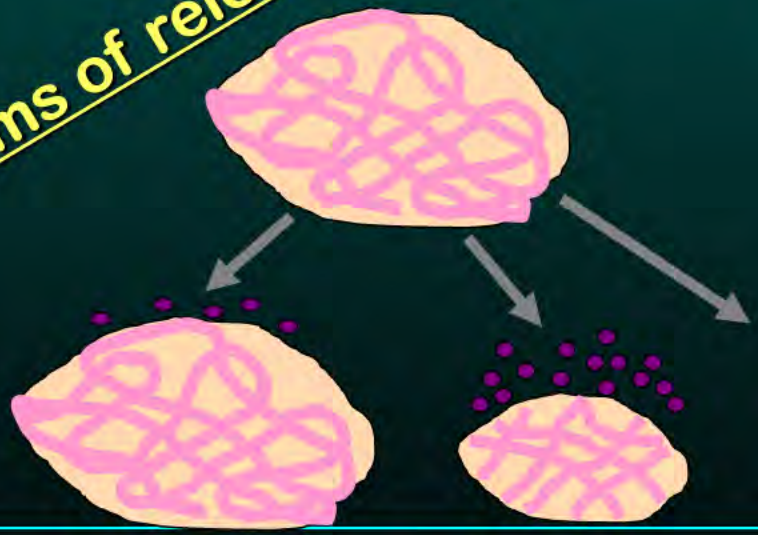
Condensation

$\equiv$Si-OH + HO-Si$\equiv$ $\rightleftharpoons$ $\equiv$Si-O-Si$\equiv$ + H_2O

$\equiv$Si-OR + HO-Si$\equiv$ $\rightleftharpoons$ $\equiv$Si-O-Si$\equiv$ + ROH

Si-O-Si: Silicon Oxide

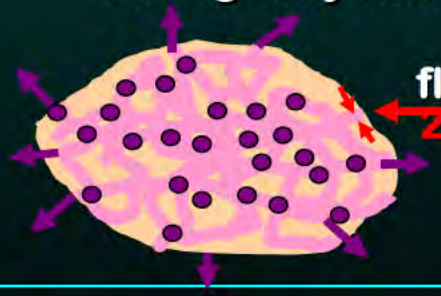
Mechanisms of release



Desorption

Resorption

Biologically active molecules diffuse out



fluid penetrates 2 nm size pores

Diffusion

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Vision

Create and build
a market leading, specialized
controlled release company

Current focus

Resistant infections

Xero-syn®

Xero-duo®

Xero-micron®

Xerogel technology

fluid penetrates
2 nm size pores

drug molecules
diffuse out

Product benefits

- Breakthrough technology
- Major unmet clinical needs
- Major health care cost savings

Strategy – Enterprise building

Product concepts for infection prophylaxis and treatment

- *Xero-syn®*
  - » *Microparticle* for surgical use
  - » Shorter regulatory pathway; near term to market
- *Xero-duo®*
  - » *Injectable nanoparticle* formulation for controlled release of two mutually complementary antibiotics for the treatment of *MRSA*
  - » Longer regulatory pathway
  - » More universal use than *Xero-syn®*
  - » Regulatory (US): Qualified Infectious Disease Product (QIDP)
    - Eligible for fast track designation
    - Priority review for marketing applications
    - Additional 5 years exclusivity granted at time of approval
- *Xero-micron®*
  - » Micron thin films on implants for continuous local delivery of bactericidal molecules
  - » Unique product concept for strategic partnering
  - » Extensive preclinical studies (rats, rabbits, sheep) as a basis for regulatory review (510(k) clearance with IDE clinical studies, or approval)

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Investment highlights

- Major markets with unmet needs
- Expansion of indications (and therefore sales) easily possible
- Extensive proof-of-concept data
- Strong IP
- Platform technology enabling enterprise building
- Potential multiple revenue streams
- Strong science and technology as a basis for strategic partnering with the device, and the biotech/pharma industry
- Multiple exit opportunities
  - » Acquisition
  - » Asset sale
  - » Partnering
  - » IPO
- Favorable comparables
- Experienced founding management; serial entrepreneur

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Conclusions
The academic mission
"Some concluding thoughts for academia"(*)

- The overall objective of academic institutions is to create and disseminate knowledge
- Tenure reviews and annual merit reviews should include metrics related to innovation
- A technology transfer relationship between centers of higher learning and their corporate offspring is confined in time (similar to: educational relationship between the institution and its students occurs over a finite time span)

(*) "Innovation through knowledge diffusion: University Based Entrepreneurship in the U.S. National Academy of Sciences September 2006

Opinion of the League of European Research Universities

Growth, research-intensive universities and the European Research Council (2005)

- *…….*
- *In research, Europe has too long adhered to a defunct model of research utility. It must recognize that the transition to a globally competitive, innovation - driven economy necessarily depends upon the stimulation of fundamental research and its link to the innovation process*
- *….*
- *Europe has permitted many of its once great research universities, which have the potential to be by far the most effective engines of fundamental research, to suffer relative decline. The re-emergence and strengthening of internationally competitive research universities as centres of excellence and innovation is crucial to Europe's competitive and cultural future.*
- *….*

Thank you