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In vitro Analysis of Scaffold/Cell Products
Tengion Autologous Neo-bladder Construct

06-07 December 07

National Transportation and Safety Board (NTSB)
490 L'Enfant Plaza East, SW
Washington, DC 20594

Integrated Technology Platform
Potential treatment of organ failure

Patient's own cells and biodegradable scaffolds

Extensive animal data-base (published and GLP)

Academic clinical experience with 6-year follow-up

Neo-organs catalyze the body's ability to regenerate

Urinary neo-bladder clinical studies underway

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Neo-Bladder Regulatory Overview
Phase 2 program ongoing

Three phase 2 studies ongoing

- *Patients with bladder failure*

Evaluation of other potential populations

- *Unmet medical need driven*

Phase 3 regulatory strategy

- *FDA interactions on clinical plan*
- *Planning based on supportive clinical data*

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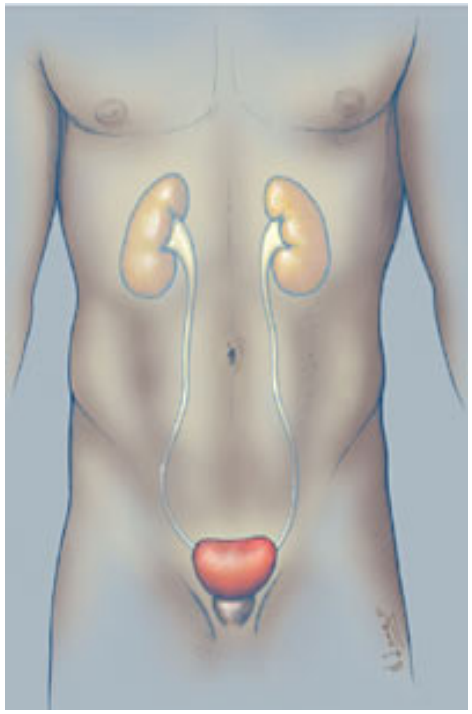
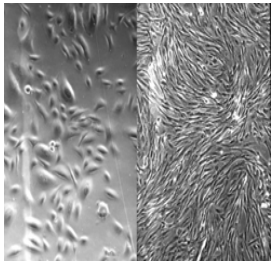
Autologous Neo-organ Development
A Unique Integrated Technology Platform



Surgeon sends patient's biopsy to Tengion.



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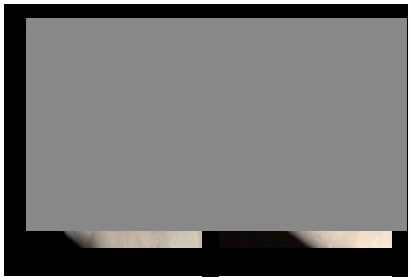
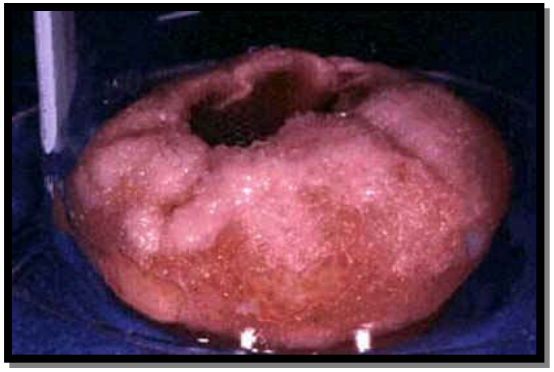


Autologous Cell source:
- No immune rejection
- Rapid tissue integration



Surgeon implants the neo-organ which regenerates.

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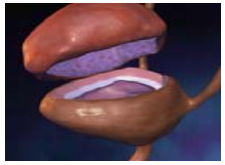
Development Program

Regenerative medicine

Biopsy/Source

Cell Expand and Seeding

Implantation



Preclinical program – Translational medicine

- *Safety and functionality*
- *Biomaterials/Bioprocess*

PMC – Process control

- *Biomaterial*
- *Cell processing*
- *Product Purity, Characteristics, Fitness-for-use/Potency*

Clinical program – Toleration and efficacy

- *Exploratory*
- *Confirmatory*
- *Post-marketing surveillance*

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Establishing Reproducibility of Bioprocess

Experimental:

- *Product and process definition, scope and scale.*

Clinical:

- *Establish product safety and efficacy using a consistent and defined process.*

Commercial:

- *Consistent production en mass - scaling up a process that worked in clinics and is cost sensitive, regulatory compliant and consistent.*

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Product Production: Scaling up

Neo-organ Production

Neo-organ production

In vitro testing

In vivo testing

GLP preclinical testing

Clinical testing

Research Labs

Labs (PCL)

Unit (CPU)

Manufacturing / Commercial

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Potential approaches to product characterization
New Assay yet to be validated

Destructive/Non-destructive

Cell Function Analysis

- *Differential cell function in mixed populations*
- *Gene Expression*

Non Destructive

Imaging

- *Micro Imaging*
  - *Quantitative tracking of cell morphology/function in culture*
  - *Visualize cells in construct*
- *Macro Imaging*
  - *Characterize construct (3D rendering)*

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Application of in vitro methods to combination product

Summary of Regulatory and Development Pathway

Tengion's Neo-bladder augment is regulated via leadership of CBER in collaboration with CDRH for BLA product registration.

- *cGMP/GTP guidelines generally apply to the manufacture of cell/scaffold combination products - 21 CFR 210, 21 CFR 211, 21; CFR 600s (i.e. 21 CFR 610), and 21 CFR 820*

In vitro test panel assess quality attributes, identity, purity, functionality, and suitability for intended use.

- *Characterization of raw materials/final product with specific QC tests*
- *Test specifications ensure product consistency and performance of the manufacturing process and product.*

Challenges include environmental, raw material and individualized product development.

- *Potential new bio-analytical approaches include non-destructive test methods that work for closed systems and customized medical products*

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