Cell expansion using Xuri W25

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Senior Program Manager

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Presented at 8th Technical Meeting of the Advanced Therapy Medicinal Product (ATMP) Manufacturing Community

Imagination at work.
Cancer Immunotherapy Named ‘Breakthrough of the Year’

The New York Times

December 9, 2012

In Girl’s Last Hope, Altered Immune Cells Beat Leukemia

By DENISE GRADY
PHILIPSBURG, Pa. — Emma Whitehead has been bounding around the house lately, practicing somersaults and rugby-style tumbles that make her parents wince.

Chimeric Antigen Receptor-Modified T Cells in Chronic Lymphoid Leukemia

David L. Porter, M.D., Bruce L. Levine, Ph.D., Michael Kalos, Ph.D., Adam Bagg, M.D., and Carl H. June, M.D.

Penn Med’s Carl June discusses breakthrough cancer research

Carl June talks to the DP about his team’s new T-cell immunotherapy treatment

The New York Times

Cell Therapy Shows Promise for Acute Type of Leukemia

Dr. Remer J. Brentjens, left, and Dr. Michel Sadelain at Memorial Sloan-Kettering Cancer Center in New York on Tuesday

By DENISE GRADY
Published: March 20, 2013  |  121 Comments
### Key Requirements of Cell Therapy Manufacturing Processes

| Scalable | Sample contained in 1 vessel  
Easy to scale out to make most efficient use of manufacturing space |
<table>
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<tbody>
<tr>
<td>Automatable</td>
<td>to minimize the chance of human error</td>
</tr>
<tr>
<td>Single Use</td>
<td>to eliminate cross contamination with other patient cells</td>
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<tr>
<td>Closed</td>
<td>system to eliminate chance of contamination with adventitious agents due to handling</td>
</tr>
<tr>
<td>Robust and Compliant</td>
<td>to ensure consistency of product and satisfaction of regulatory requirements</td>
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*One patient, one sample, one chance…………*
Our approach: A cell therapy dose in a single Cellbag

Xuri Cell Expansion System W5
Formerly WAVE Bioreactor System 2/10

Xuri Cell Expansion System W25

Generation of 20 billion cells

Viable Cells

Days of culture

= 100 x

10^{11}
10^{10}
10^{9}
10^{8}
10^{7}
0 2 4 6 8 10 12 14
Single-use Cellbag Bioreactor

- Oxywell2 port
- Y dip tube for Perfusion harvest
- Needleless sampling port
- Outlet air filter
- Inoculation/Feed line
- Spare luer port / optional pH probe
- Inlet air filter
Xuri™ Cell Expansion System W25

- Robust and reliable
- Control over critical cell culture parameters
- CFR Part 11 compliant
- GAMP 5
- Expandable for integration of new technologies
- Service and support
- UNICORN™ software with an intuitive, graphical interface
Minimise risk of sample loss
Process monitoring and remote operation

Remote control of 3 units simultaneously
Remote monitoring of 32 units from one computer.
Email notifications
Optimization Studies: WIP system control

Objective: Maximize the expansion of viable T cells in a 10 day period

Optimized speed and angle: 15 rpm, ~6°, increased yield

<table>
<thead>
<tr>
<th>Speed (rpm)</th>
<th>2</th>
<th>2</th>
<th>10</th>
<th>10</th>
<th>10</th>
<th>10</th>
<th>18</th>
<th>18</th>
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<tbody>
<tr>
<td>Angle (°)</td>
<td>6</td>
<td>9</td>
<td>2</td>
<td>6</td>
<td>9</td>
<td>2</td>
<td>6</td>
<td>9</td>
<td></td>
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<tr>
<td># of expts</td>
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<td>1</td>
<td>1</td>
<td>1</td>
<td>5</td>
<td>1</td>
<td>1</td>
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Understand Phenotype

QC analysis

Phenotype monitoring of:
- CD4/CD8 ratio
- CD27/CD28 expression to assess differentiation state
- CD57 expression to assess the presence of senescent cells
- CD62L expression to assess migratory ability
Summary

- Autologous cellular immunotherapies have unique scalability requirements
- Xuri™ W5 and W25 expansion systems provide robust and reliable expansion of functional T cells
- Higher cell densities and a closed and automated system make them ideal for therapeutic use

Xuri Cell Expansion System W25 enhanced features to help you progress the production of cells from clinical research to commercial manufacturing.

Xuri Cell Expansion System W5 particularly suitable for translational research laboratories.
Xuri™
Believe in better futures

www.gelifesciences.com/xuri
Thank you.

Xuri W25 This is not a medical device nor CE marked and should not be used in diagnostic processes. Drug manufacturers & clinicians are responsible for obtaining the appropriate IND/BLA/NDA approvals.

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Xuri W25 Configuration

**Xuri W25 Base unit**
Base unit with internal controller, hard drives, heater, and scale

**Xuri Pump 25**
Pump module

**Xuri CBCU**
Gas mixer, pH, and DO control

**UNICORN™ software**
Software installed on customer PC