Capacity Planning Considerations for Autologous Cell Therapies

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Agenda

• 3 general challenges that make capacity difficult

• Unique challenges for autologous cell therapy

• Addressing the challenges
Patient Cell Journey – Autologous therapies

**Time to Treatment**

In general, ~3-4 Weeks between apheresis and treatment
General Challenges

- Inventory
- Scaling
- Communication
What’s one the most foundational differences? - Inventory buffer

<table>
<thead>
<tr>
<th>Inventory Type</th>
<th>Individualized Therapies</th>
<th>Biologics/Small Molecules</th>
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</thead>
<tbody>
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<td>Raw Materials</td>
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<tr>
<td>Drug Substance</td>
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<tr>
<td>Drug Product</td>
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<td>✓</td>
</tr>
<tr>
<td>Finished Goods</td>
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<td>✓</td>
</tr>
<tr>
<td>Channel</td>
<td></td>
<td>✓</td>
</tr>
</tbody>
</table>

*Planning, alignment, and communication are critical
Scaling: Fundamental difference in make to order vs make to stock
Foundational things you’ve always done must be more tightly integrated than ever before

Small blips can make huge waves

Mis-alignment can directly impact patients

It will be more complex than you think

It will take longer than you plan

Unexpected things will happen
Unique challenges that can impact autologous cell therapy capacity

**Turnaround Time**
- Patient is part of Supply Chain
- Time from vein to vein is critical: white glove service needed
- Hospital/treatment center capacity constraints become yours
- Tied to your Mfg capacity

**Manufacturing & Materials**
- Labor intensive & manual
- Ramping capacity requires long lead time
- Storage capacity is critical
- Robust supply chain needed
- Nascent suppliers/CMOs - their capacity is your capacity
- Patient’s cells are starting material with unknown variability

**Systems & Interfaces**
- Must have strong integration between systems
- Manual operations will reduce capacity and be costly

**Regulatory**
- Prior Approval required to increase capacity (add identical unit operations)
- Need plans in place to manage out-of-specification drug product

**People**
- People capacity will be consumed by execution tasks
- Burnout

**Quality**
- Rapid release is essential
- Must be Right First Time
- Quality operations must ramp in step with Mfg.
How to address the challenges

**Turnaround Time**
- Treat as a value stream
- Know what’s achievable now vs. future
- Find predictive tools: proactive vs. reactive

**Manufacturing & Materials**
- Automation & manage capacity as a program
- Select the right suppliers & materials early
- Share forecasts & partner
- Design your manufacturing facilities for the highest level of flexibility
- PLAN & hire early

**Systems & Interfaces**
- System implementations & builds must happen quickly and be well integrated
- Must have strong integration between IT/Commercial/Operations

**People**
- Need ops execution as a stand-alone organization
- Org design & programs for business continuity
- Automate

**Regulatory**
- Incorporate clear, complete Post Approval Change Management Protocol for capacity into BLA
- DP OOS: Seek approval for Expanded Access Protocol (EAP) in parallel with BLA review

**Quality**
- Automate
- Plan and hire early
- Robust testing chain required
What’s the next bottleneck?

- Harmonize and have consistency across nodes as you increase your capacity or that will impede ability to scale & grow.
- Complexity is here now, even if you think you have time to figure it out.

*It will be more complex than you think*

*It will take longer than you planned*

*Unexpected things will happen*
In Summary:

- **PLAN & Re-plan**
- **Communicate and Align to plans**
  - Create programs to govern and drive things like manufacturing capacity ramps & turnaround times
  - Hire early
  - Be realistic, employ defensive pessimism
  - Always do what’s best for patients