

Cell & Gene Therapies

Leveraging Manufacturing IT Systems to boost efficiency and compliance in autologous Cell & Gene Therapy

Clinical Supply Forum, Leiden, Dec 13, 2019

Cell & Gene Therapies

CNN FDA approves gene therapy for a type of blindness



MIT Technology Review Gene Therapy Is Curing Hemophilia

Novo Nordisk expands cell therapy R&D, says type 1 diabetes cure a step closer

Company has reached milestone in stem cell therapy as it looks to broaden range beyond diabetes

Science Gene therapy's new hope: A neuron-targeting virus is saving infant lives

DER SPIEGEL

E Erste Gentherapie gegen Krebs

"Eine neue Ära der Leukämiebehandlung"

D Die erste Gentherapie gegen Krebs steht kurz vor der Zulassung. Bei der Therapie attackieren eigene, manipulierte Immunzellen die Krebszellen im Körper - allerdings mit gefährlichen Nebenwirkungen.

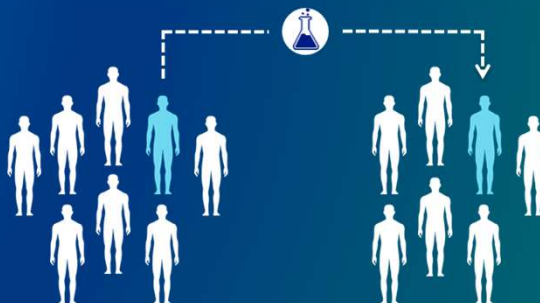


THE PARADIGM SHIFT

Therapy Options

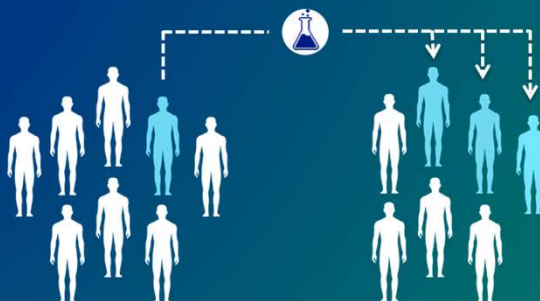
Autologous therapy

Donor's cells are used to build a therapy specifically for the donor (1:1 relation)



Allogeneic therapy

Donor's cells are used to build therapies for a group of recipients (1:n relation)

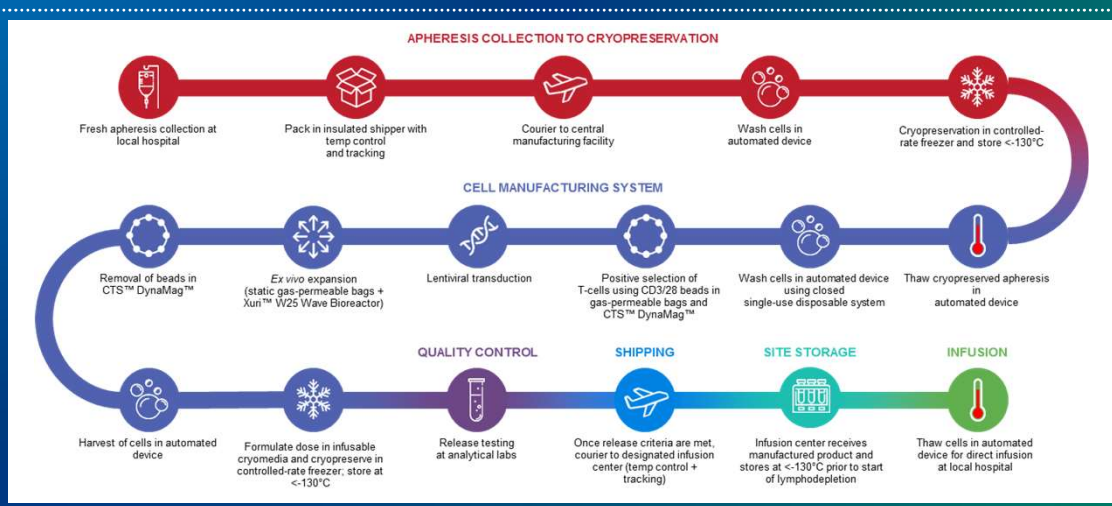


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Patient cell journey in the Autologous Process – One patient, One batch



Source: John Linger, Adaplimune, at CAR-T Summit Boston, 2019

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Addressing Supply Challenges in C&G therapies

- Speed
 - From patient identification/qualification to start of manufacturing
 - “Vein-to-Vein” time from apheresis to infusion
 - Manufacturing time
- Manufacturing scheduling complexity
- Chain of Identity / Chain of Custody management
- Scale for commercial

Source: John Lunger, Adaplimune, at CAR-TCR Summit Boston, 2019
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Speed of Therapy

Challenges

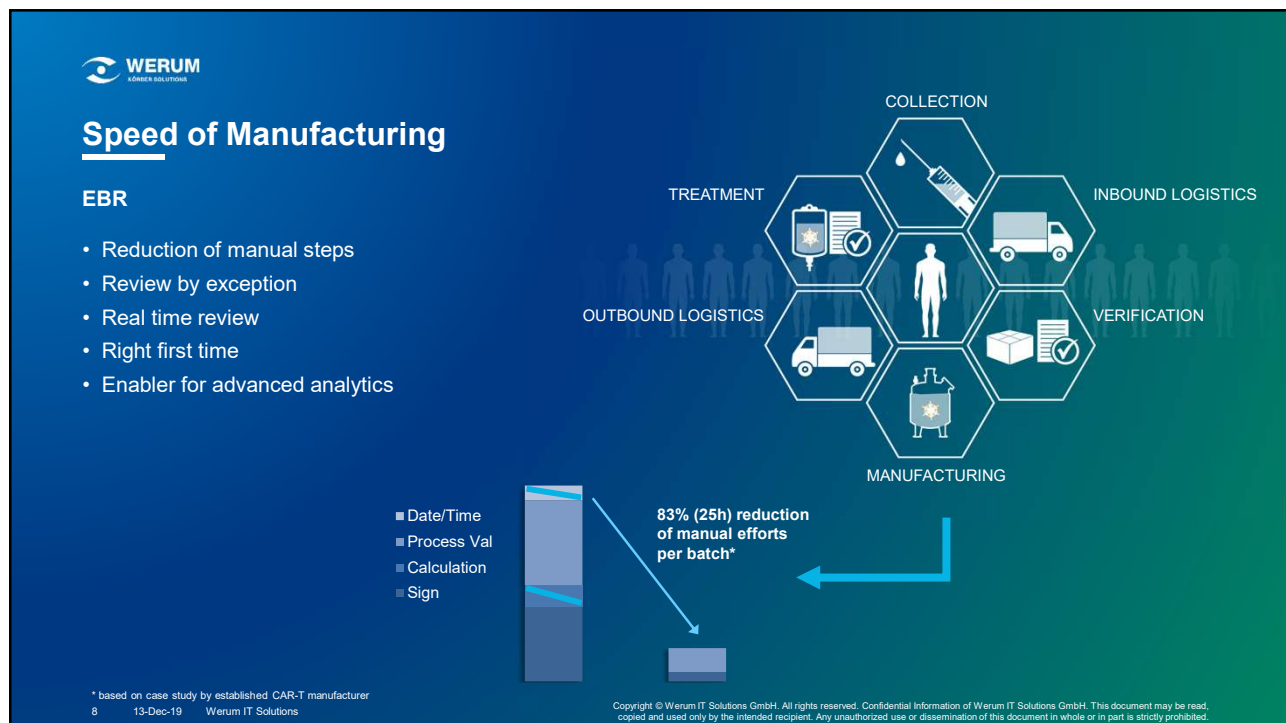
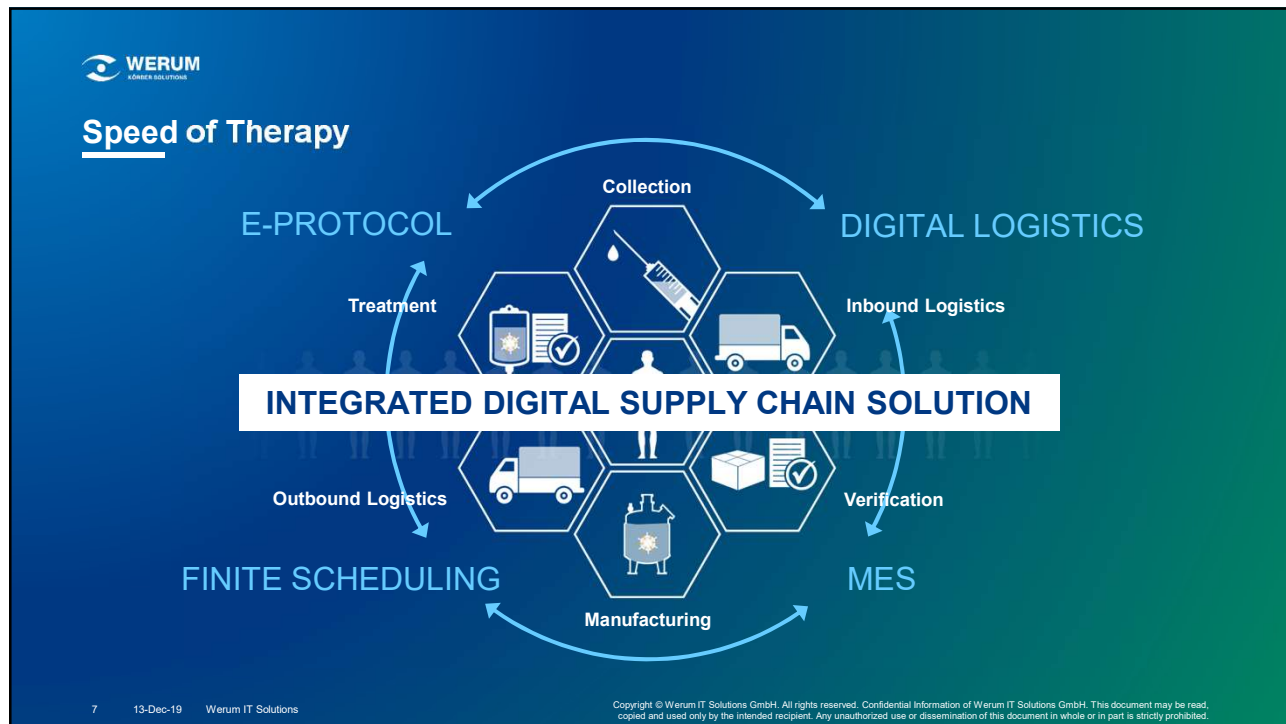
- Patient identification to manufacturing start
 - Patient qualification (screening, diagnostics)
 - Apheresis center coordination
 - Patient coordination (travel, treatment schedules)
 - Manufacturing capacity available ?
- “Vein-to-vein”
 - Manufacturing cycle times
 - QA/QC release cycle times
 - Global logistics management
 - Lymphodepletion coordination
 - Infusion coordination

Approach

- Communication and information sharing via applications and platforms
- Clinical operations management
- Robust analytics to optimize capacity planning (e.g. enable manufacturing < 7 days from patient qualification)
- Speed of manufacturing execution
 - Electronic batch records
 - Review by exception
 - Minimize deviations/excursions (e.g. close open steps)

Source: John Lunger, Adaplimune, at CAR-TCR Summit Boston, 2019
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Manufacturing Scheduling Complexity

Coordination of apheresis, manufacturing, lymphodepletion, and infusion for each patient is complex

Challenges

- Patient clinical condition may cause late changes to treatment schedules
- Apheresis unit constraints
- Treatment center capacity management
- Manufacturing resourcing and scheduling
- Unit operations scheduling and capacity planning
- Facility and equipment maintenance management (e.g. shutdowns)

Approach

- Robust long-term capacity planning based on desired “fill rates” (i.e. minimize queue time for manufacturing slot)
- Redundant/backup equipment
- Facility design for maintenance, minimize down time
- Detailed production scheduling tools
- Longer term:
 - Engage with treatment centers to support operations
 - Cell orchestration platforms for visibility beyond the “four walls” of manufacturing

Source: John Langer, Adaptimmune, at CAR-TCR Summit Boston, 2019
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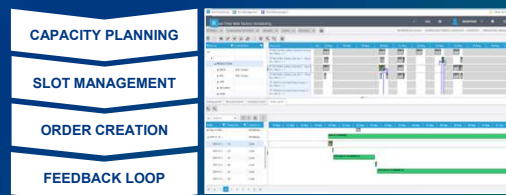
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Scheduling Complexity

Digital scheduling

- Manufacturing bottleneck identification
- Real time feedback from MES to scheduler
- Product available to promise (ATP)
- Real-time updated and visibility via system integration

Clinician - Collection - Manufacturing



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Chain of Identity / Chain of Condition / Chain of Custody (Col / CoC)

Particular focus on Col/CoC management in both clinical and commercial supply operations

Challenges

- Crucial Col/CoC for autologous product; zero risk tolerance
- Global supply, multi language (e.g. apheresis/treatment centers in one country, manufacturing in another)
- Re-manufactures (same patient, multiple apheresis, multiple doses, multiple manufactures)
- Multiple apheresis aliquots

Approach

- Implement electronic management systems early in clinical development
- Backup paper systems for Col/CoC
- Implement validated cold chain

Source: John Linger, Adaplimune, at CAR-TCR Summit Boston, 2019
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Chain of Identity / Chain of Condition / Chain of Custody (Col / CoC)

Collection



Collection and processing of patient material

Inbound Logistics



Transport to manufacturing site asap

Manufacturing



Manufacturing based on patient material

Outbound Logistics



Transport to treatment center asap

Treatment



Thawing and drug infusion



PAIN POINTS



WHICH SAMPLE BELONGS TO WHICH PATIENT?



SAMPLE TREATMENT UNDER CORRECT COND.



WHO IS HANDLING THE SAMPLE?



TIME IS RUNNING, LIVING ORGANISMS!



PRODUCT ID, TRACKING, MATCHING WITH PATIENT ID?



SAMPLE TREATMENT UNDER CORRECT COND.



WHO IS HANDLING THE SAMPLE?



TIME IS RUNNING, LIVING ORGANISMS!



LINKAGE OF THE NEW PRODUCT TO THE RIGHT PATIENT? ERROR FREE WORKFLOWS UNDER RIGHT COND.



WHO IS HANDLING THE SAMPLE?



TIME IS RUNNING, LIVING ORGANISMS!



PRODUCT ID, TRACKING, MATCHING WITH PATIENT ID?



SAMPLE TREATMENT UNDER CORRECT COND.



WHO IS HANDLING THE SAMPLE?



TIME IS RUNNING, LIVING ORGANISMS!



THE RIGHT PRODUCT FOR THE RIGHT PATIENT?



SAMPLE TREATMENT UNDER CORRECT COND.



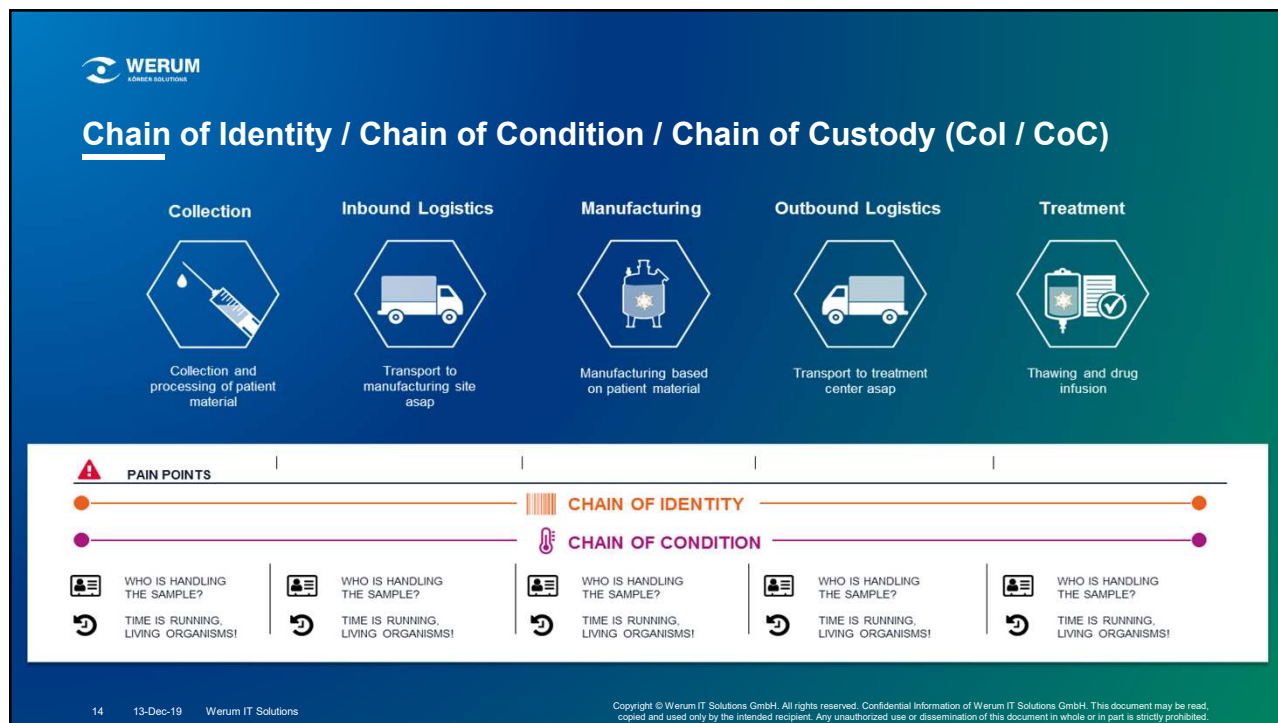
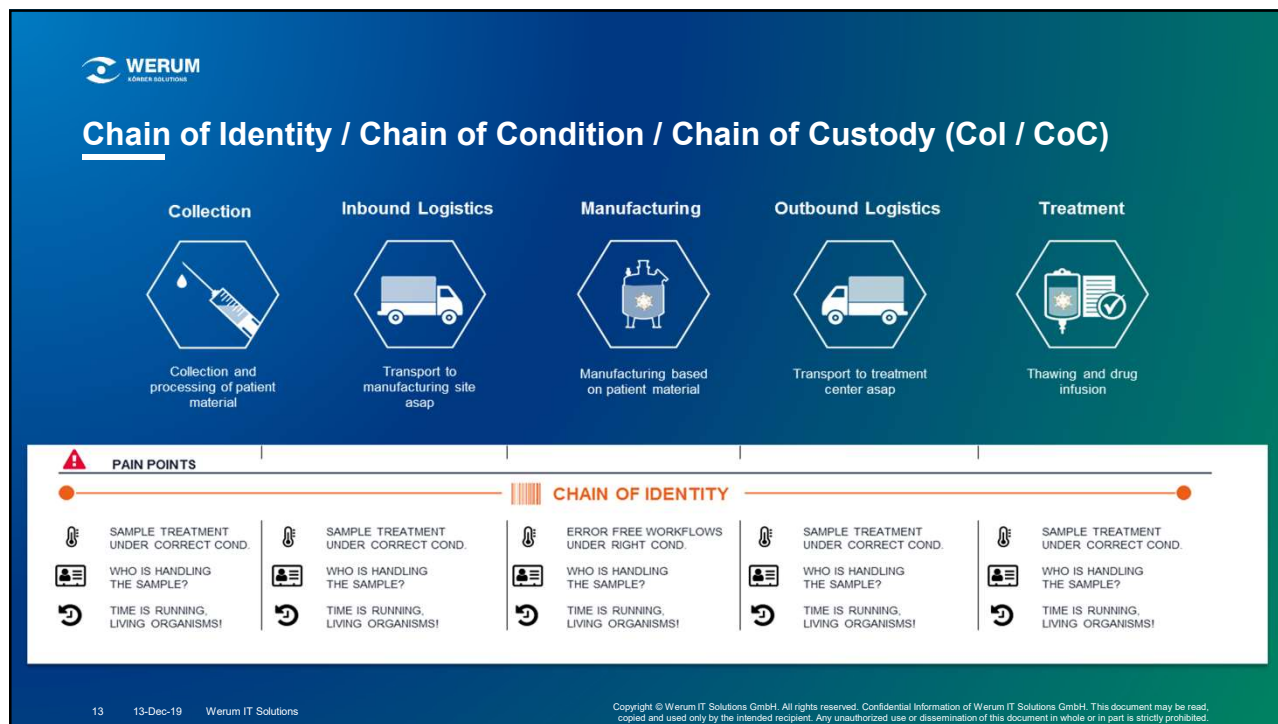
WHO IS HANDLING THE SAMPLE?

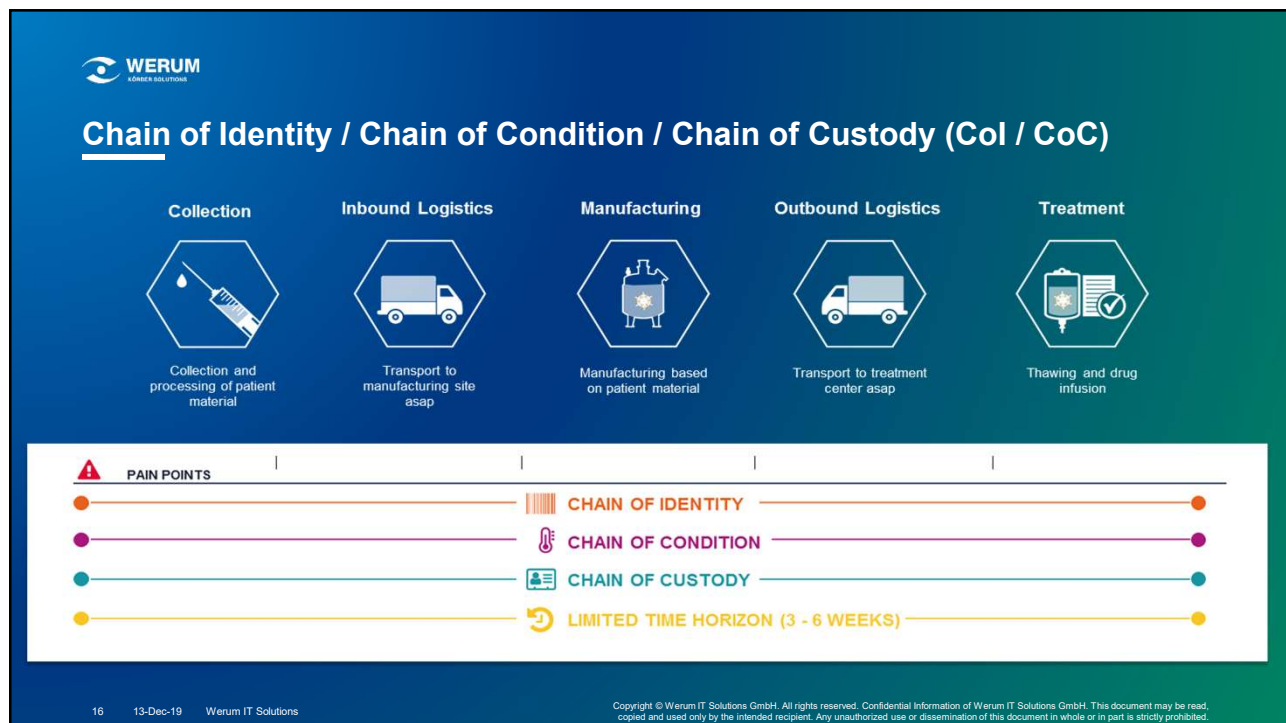
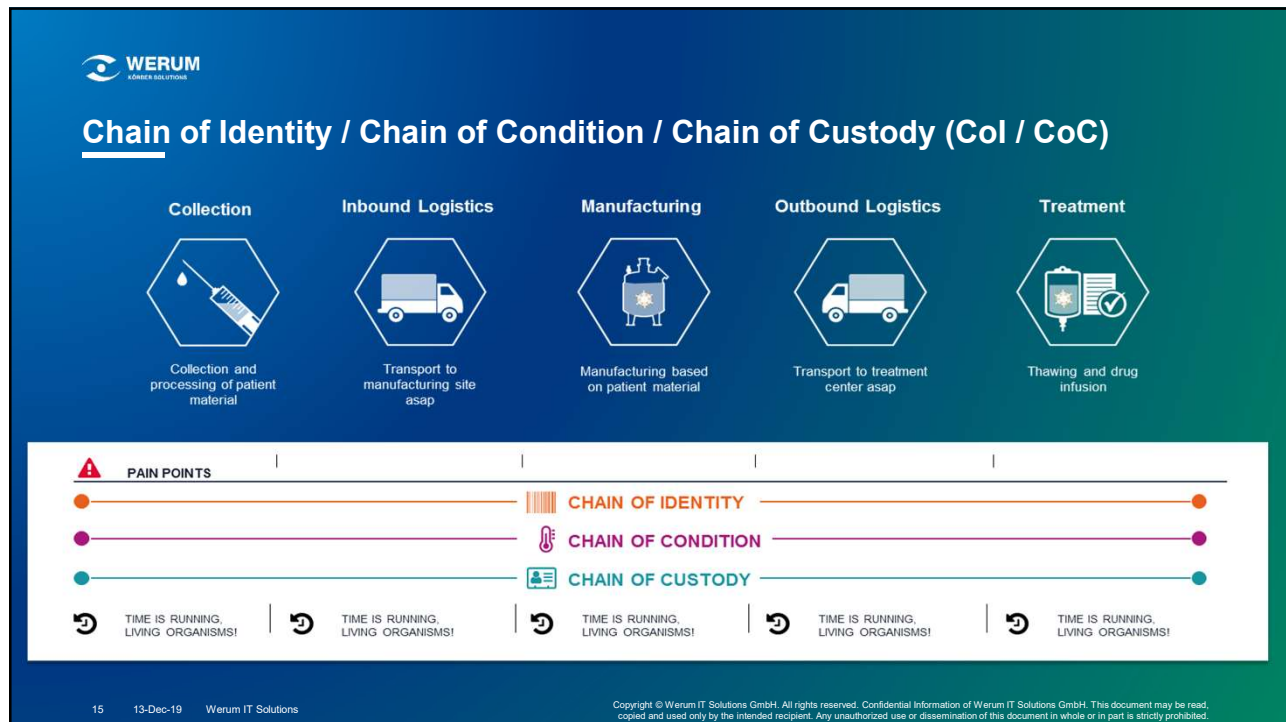


TIME IS RUNNING, LIVING ORGANISMS!

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Scale for Commercial

Moving beyond the scale of a clinical trial has unique challenges

Challenges

- “Scale out” vs. “Scale up”
 - more batches, not larger batches
- Manufacturing network optimization decisions
 - Regional → global, centralized → distributed
 - Long range capacity planning
- Clinical vs. commercial supply operations management
 - Much more overlap in patient operations than in traditional biopharma
- Multi-language operations
- COGS

Approach

- Early implementation of information systems
- GMP, validated, scalable infrastructure
- Earlier focus on efficiency than with typical new product launch
- “Patient operations” common across clinical and commercial programs

Source: John Langer, Adaplimune, at CAR-TCR Summit Boston, 2019
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Cell & Gene Solution for commercial manufacturing at scale

- Move away from complex paper based systems
- Automate manual process and review steps
- Integrate electronic systems from collection, logistics, manufacturing through treatment
- Establish end-to-end visibility

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Cell & Gene Solution for commercial manufacturing at scale

OUR FOOTPRINT IN CELL & GENE THERAPY MARKET

NOVARTIS Adaptimmune
PCT Cell Therapy Services, LLC
A Hitachi Group Company
J.W. Therapeutics
Kite Takeda BRI ATARA BIO

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