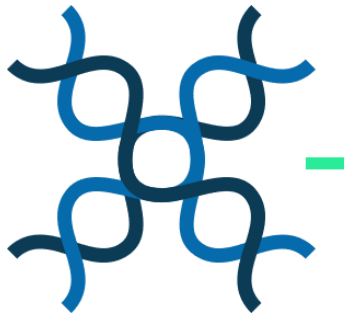


OPEN
-CELLERATOR
COMMUNITY

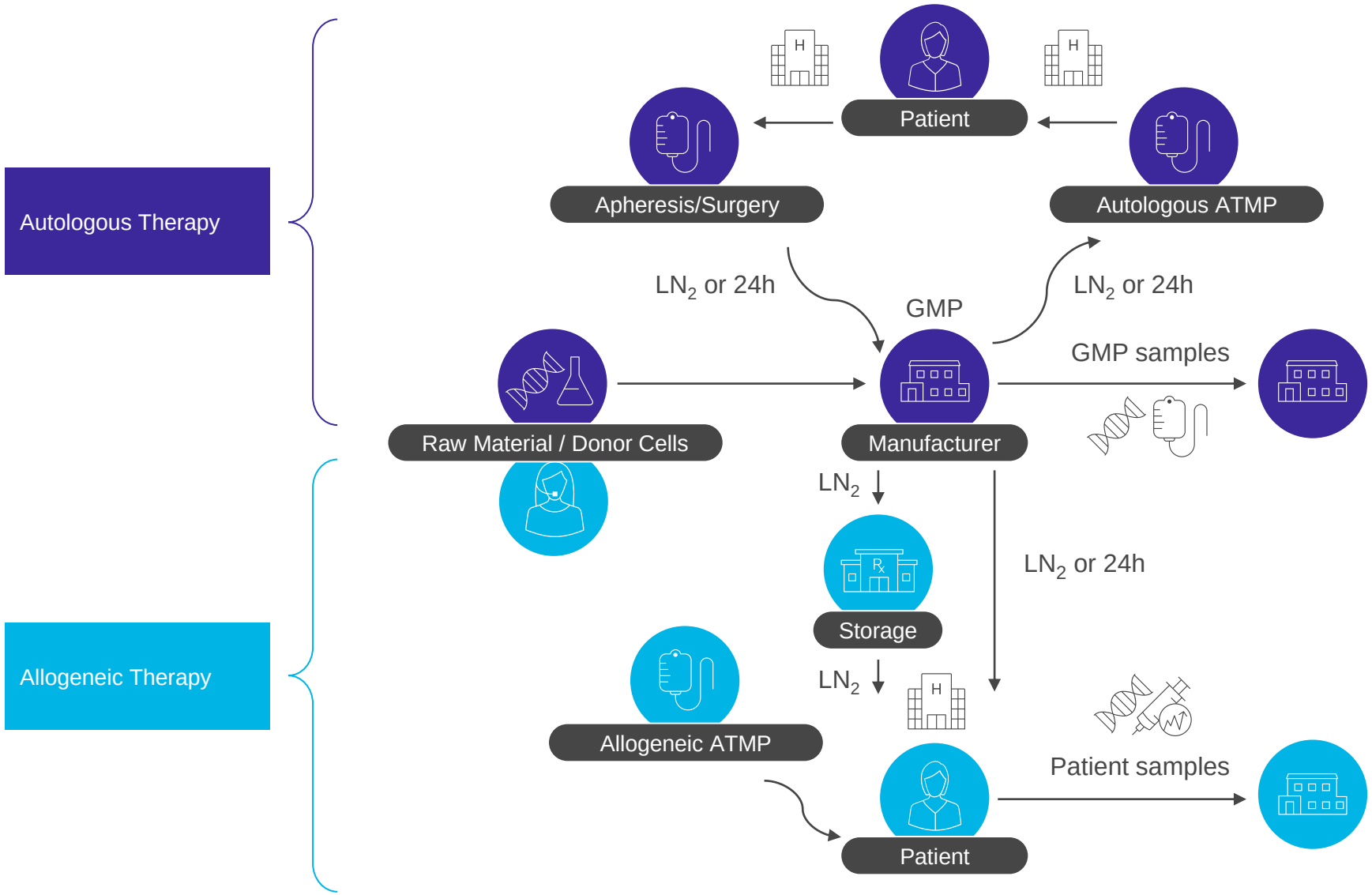
AmerisourceBergen
World Courier

Transportation: What it means to be one point globally

Dr. Andrea Zobel, Senior Director
Personalized Supply Chain

23 September 2021

Logistics platforms for autologous and allogeneic supply chains



Autologous therapies have availability and logistics challenges

Medical advantage:

- No immune reaction and graft vs host disease

Availability challenges:

- Quantity/quality of cells often poor
- Limited quality testing
- Manufacturing capacity and sites
- Regional vs global availability

Logistics challenges:

- Reaching limitations
- Short shelf life below 30 hrs
- Expanding shelf life – only possible at -196°C
- Two time and temperature critical supply chains
- Traceability

Allogeneic therapies have logistics challenges too, but bigger potential to scale

Advantages:

- Optimal cells from selected donors
- Standardized products
- Expansion of dose numbers
- GMP-compliant testing
- Immediate availability
- Eliminated risk of immune response through 2nd generation products

Medical challenges:

- Risk immune reaction and graft vs host disease

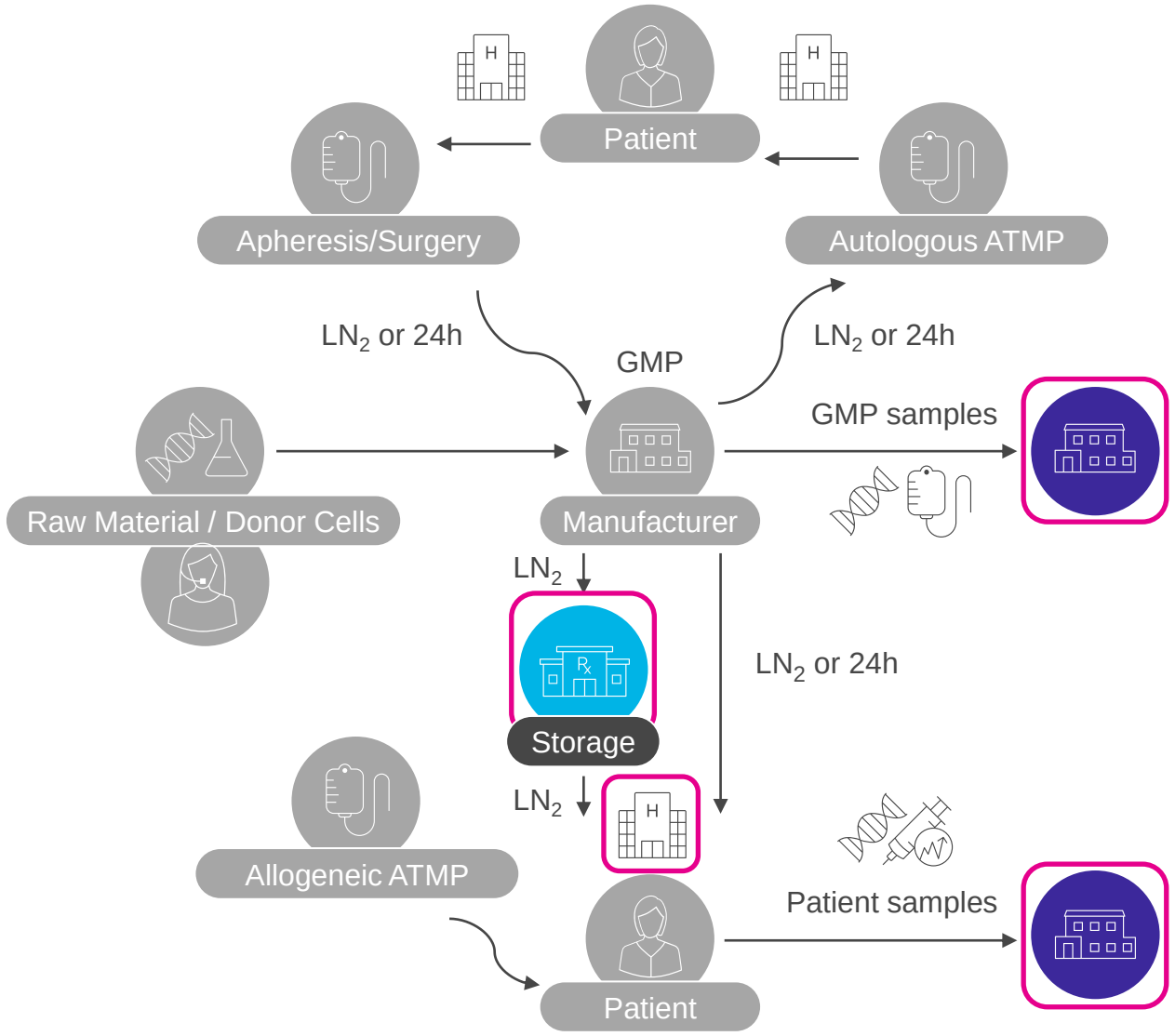
Logistics challenges:

- Short shelf life 30 to 72 hrs
- Expanding shelf life – only possible at -196°C
- Global cryogenic supply chain required

Cryogenic storage is a supply chain requirement

Autologous Therapy

Allogeneic Therapy



Transportation of cell & gene therapies is highly regulated

EU guideline on Good Clinical Practice Specific to Advanced Therapy Medicinal Products requests tight controls of:

- Storage and distribution
- Traceability
- Temperature control


EUROPEAN COMMISSION

Brussels, 10.10.2019
C(2019) 7140 final

GUIDELINES

on Good Clinical Practice specific to Advanced Therapy Medicinal Products

(Text with EEA relevance)

"Storage, transport and handling conditions have the potential to negatively impact the quality of ATMPs. The sponsor should provide the investigator with detailed instructions for the handling and storage of investigational product(s) in the clinical trial site. Where the ATMP requires controlled temperature conditions during transport and/or storage prior to administration, **the sponsor should ensure there is a temperature monitor/ log data and/ or confirmation that required conditions have been met**"

"For example, manufacturing constraints and the short shelf-life of the product may require the implementation of tight controls on logistical arrangements to administer the product."

ISO 21973:2020 General requirements for transportation of cells for therapeutic use

GUIDANCE DOCUMENT

Chemistry, Manufacturing, and Control (CMC) Information for Human Gene Therapy Investigational New Drug Applications (INDs) *Guidance for Industry*
JANUARY 2020

"Proper control of the finished DP is critical to your investigational studies. Therefore, your IND should include a description of how the product will be shipped to, received, and handled at the clinical site to ensure safety, product quality, and stability. **Your IND should also include information on shipping conditions, storage conditions, expiration date/time (if applicable), and chain of custody** from the manufacturer to the site of administration in the summary information of the CTD. "

Cellular & Gene Therapy Products | FDA

A range of cryogenic shipping options for all requirements

VIA Capsule

Unique LN_2 free technology with inbuilt tracking

- Ideal for users not familiar or
- not permitted to use LN2
- Extended storage at treatment center, powered by electricity
- Shipper of Cytiva's cell therapy system

SAVSU

Smart shipper with inbuilt tracking

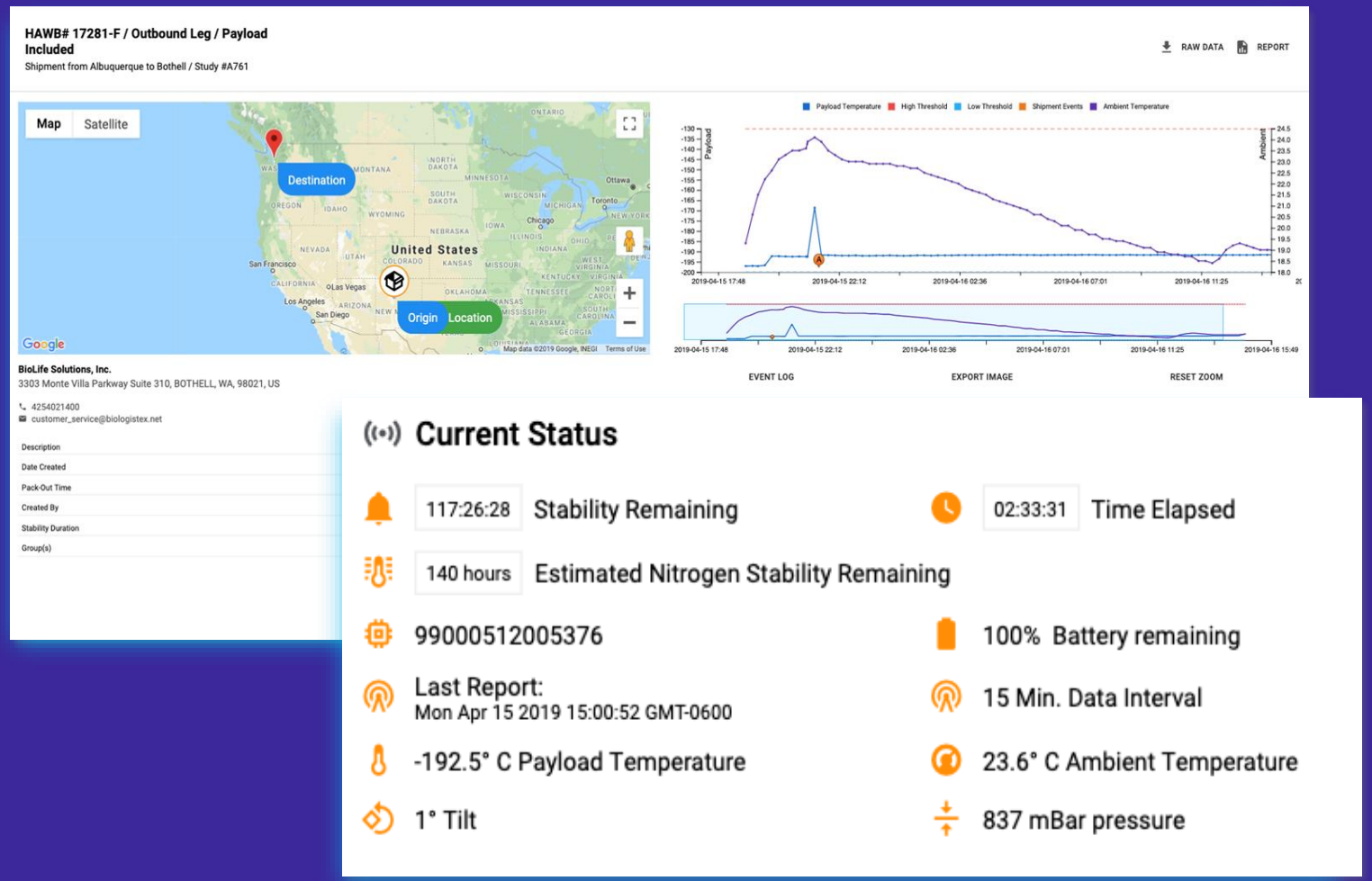
- Designed for all standard cell and gene therapy packages
- Qualification period is 10 days

Palletized MVE

Established, widely used dry shipper

- Suitable for large quantities
- Qualification period is 10 days

Real time tracking & reporting required



SAVSU

Smart shipper with inbuilt tracking

- Site users can verify current temperature without accessing a website
- Blinks for out of range; displays solid for in range.
- Real time temperature reading if shipper can't access cellular network.
- Simplified one button design prevents confusion

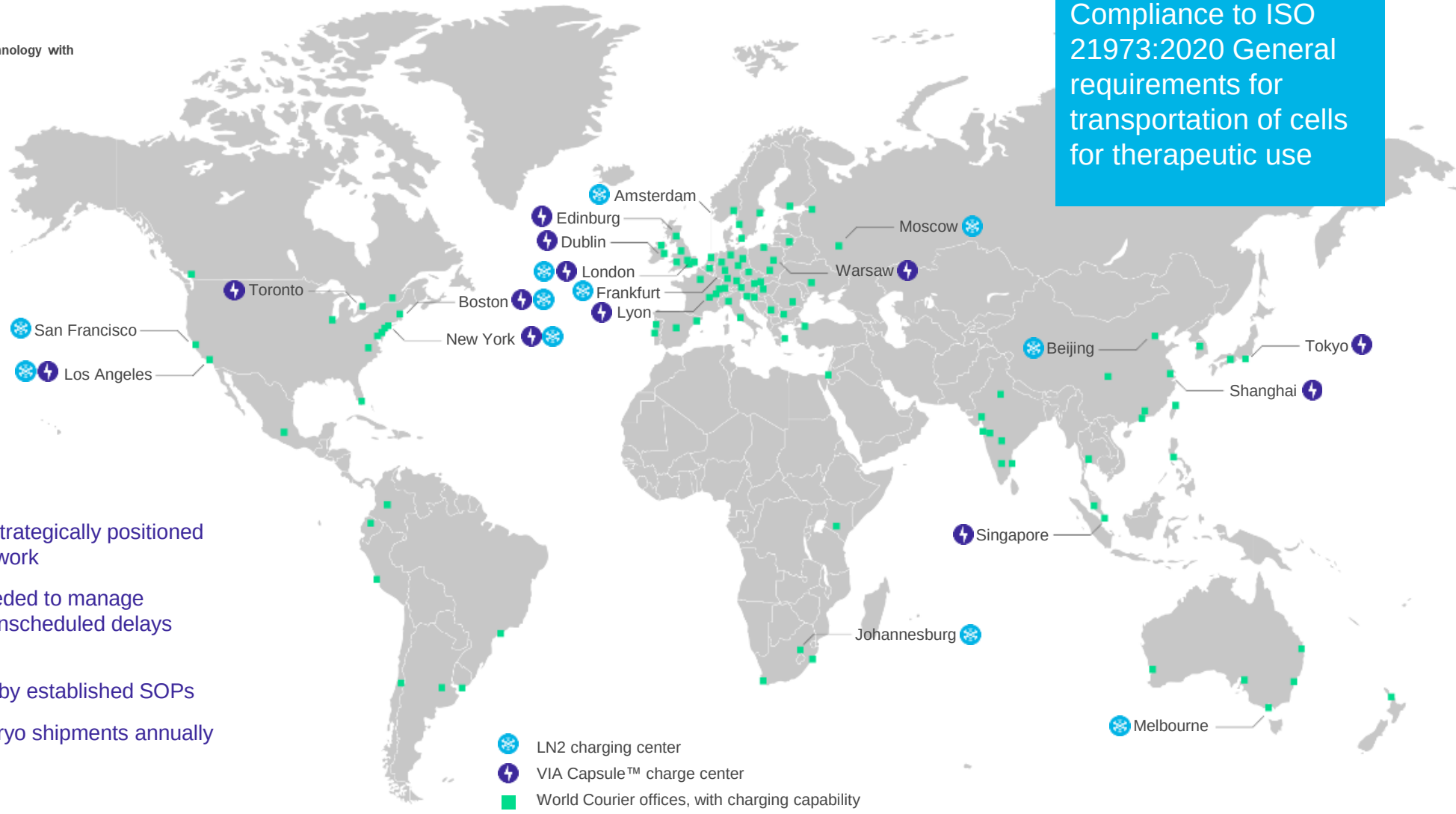
savsu TECHNOLOGIES

Global cryogenic shipping management and charging capability

VIA Capsule
Unique LN_2 free technology with inbuilt tracking

SAVSU
Smart shipper with inbuilt tracking

Compliance to ISO 21973:2020 General requirements for transportation of cells for therapeutic use



- Multiple charge stations strategically positioned throughout the global network
- Ability to intervene as needed to manage unexpected events and unscheduled delays
- Driven by a single quality system and underpinned by established SOPs
- Supporting over 10,000 cryo shipments annually

Regional differences in Gene Therapy Guidances

GMO requirements for investigational products
[Genetically Modified Organism (GMO) aspects for investigational medicinal products | Public Health (europa.eu)]

MEDICINAL PRODUCTS FOR HUMAN USE CONTAINING OR CONSISTING OF GMOS: INTERPLAY BETWEEN THE EU LEGISLATION ON MEDICINAL PRODUCTS AND GMOS

- **Are medicinal products that contain or consist of genetically modified human cells subject to the GMO framework?**
- Are medicinal products that consist of plasmids subject to the GMO framework?

Interpretation by country, not harmonized by CAT!

Genetically modified cells are considered dangerous goods with UN 3245 in EU but not in US!
Additional costs per shipment in EU!

GUIDANCE DOCUMENT

Determining the Need for and Content of Environmental Assessments for Gene Therapies, Vectored Vaccines, and Related Recombinant Viral or Microbial Products *Guidance for Industry* MARCH 2015

FDA generally considers GTVVs that consist of genetically modified human cells to be substances **that "occur naturally in the environment"** for purposes of 21 CFR 25.31(c) because these cells have stringent nutritional requirements for survival and replication and are therefore **not viable in the environment** and are degraded into naturally occurring substances.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Biologics Evaluation and Research
March 2015

CGT shipments from donation to follow-up are established during clinical phase and ready for scale-up after approval

Cost Efficiency

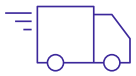
Donation

Patient or donor recruitment

Sample collection kit order

Donation collection

- Booking and hand-over processes between courier and donation centers established
- Equipment tested and ready for scale-up

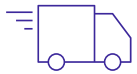


Donation transport

Therapy manufacturing

Vector

Vector manufacturing



Vector transport

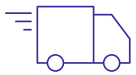
Therapy manufacturing

- Supply chain of vectors established
- Import and depot licenses available according to local regulations

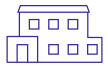
Therapy

Therapy manufacturing

Allogenic

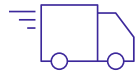


Therapy transport



Cryo store

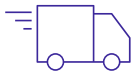
Specialty distribution



Therapy transport

Patient receipt

Autologous



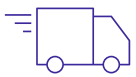
Therapy transport

- Shipment lanes, hand-over processes and schedules established between manufacturers, courier and treatment center
- Regional storage locations with sufficient capacity in required temperature ranges equipped, contracted, qualified and ready to store

Patient receipt

Monitoring (and returns)

Sample collection



Monitoring sample transport

Specialist laboratory

- Sample supply chain established and ready for long-term execution
- Transition from clinical trial laboratory processes to long-term follow-up of patients


thank you

JOINTLY CREATING THE FUTURE OF CELL & GENE THERAPY ORCHESTRATION