PDA Parenteral Drug Association

2020 PDA EUROPE

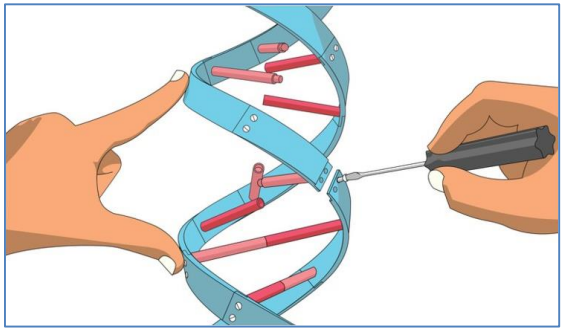
Parenteral Packaging

ARaymond MORE THAN FASTENING

SCHOTT glass made of ideas

25-26 FEBRUARY 2020
BASEL | SWITZERLAND

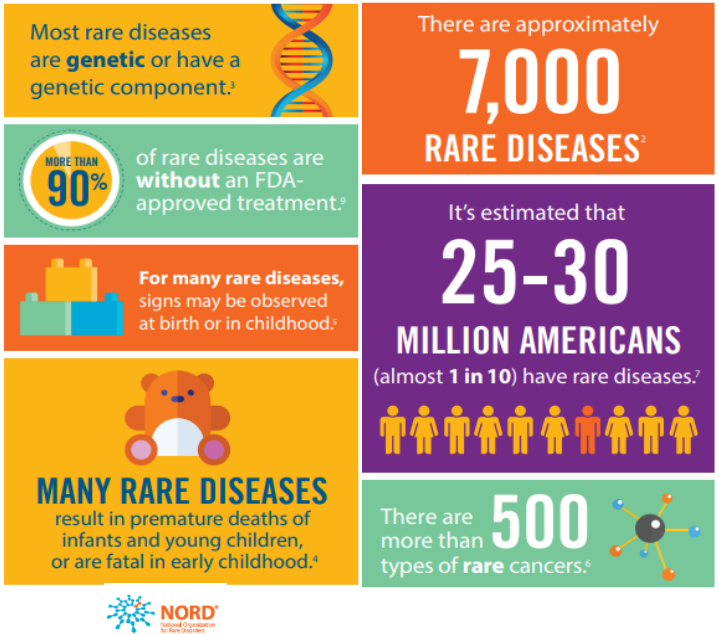
CONNECTING PEOPLE SCIENCE AND REGULATION®



SUITABILITY OF A CONTAINER CLOSURE SYSTEM FOR PACKAGING AND CRYOGENIC STORAGE OF GENE THERAPY PRODUCTS

Joint presentation ARaymondlife - SCHOTT

Rare Diseases are a growing public health concern



Source: https://rarediseases.org/get-involved/educate/raise-awareness/

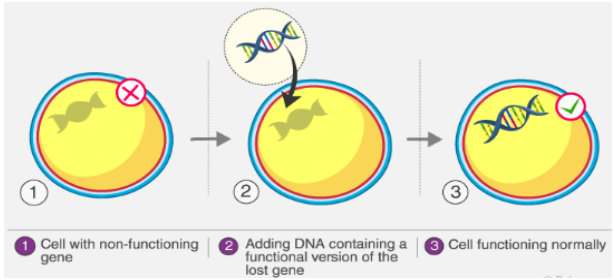
Rare Diseases Facts

- 7,000 + Rare diseases WW
- Of these, 80% are genetic diseases
- 25 - 30 million Americans
- 30 million Europeans
- 320 million people WW
- No cure for the vast majority of diseases

Focus on ATMP's definition and Gene Therapy

Advance Therapy Medicinal Products (ATMP's)

Gene therapy medicinal products

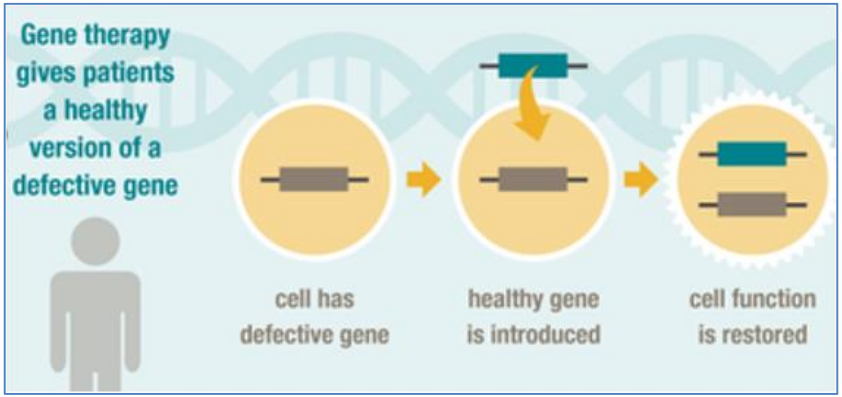


Somatic cell therapy medicinal products

Tissue engineering products

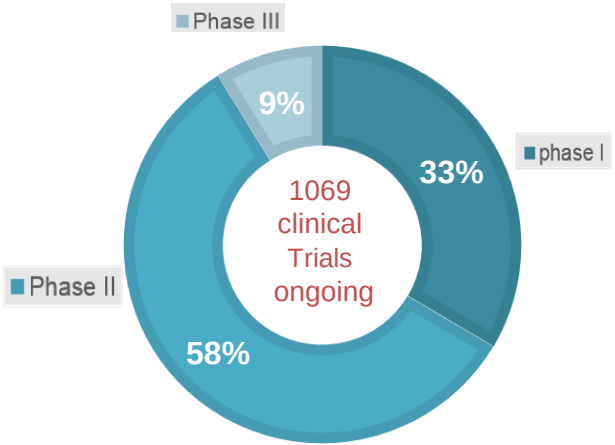
What is gene therapy ?

Gene Therapy aims to restore function and slow disease progression, which could potentially enable a patient to manage their disease without the need for ongoing treatment.



ATMP: a growing field with specific needs

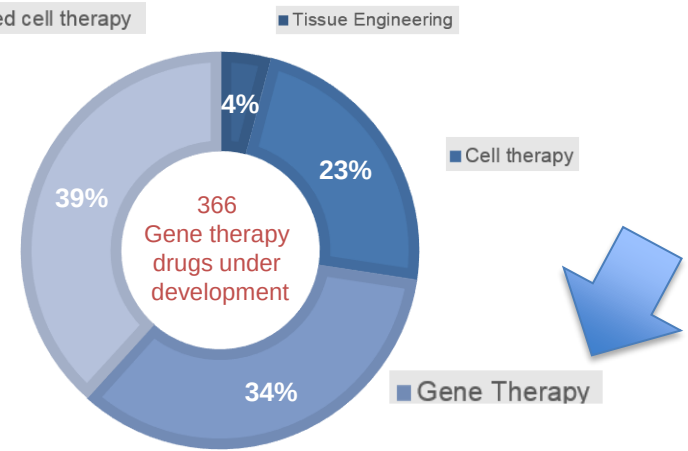
TOTAL REGENERATIVE MEDECINE CLINICAL TRIALS



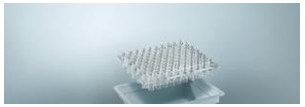
Phase 1: 358 across all tech types and indications	Gene Therapy: 117 Gene-Modified Cell Therapy: 187 Cell Therapy: 49 Tissue Engineering: 5
Phase 2: 617 across all tech types and indications	Gene Therapy: 219 Gene-Modified Cell Therapy: 207 Cell Therapy: 168 Tissue Engineering: 23
Phase 3: 94 across all tech types and indications	Gene Therapy: 30 Gene-Modified Cell Therapy: 16 Cell Therapy: 32 Tissue Engineering: 5

source: alliance for regeneratice medicines

TYPE OF PRODUCT



Gene and cell therapy are major growth opportunities for the pharma industry



Value of recent biotech company acquisitions

Company	Aquisition	Deal
Celgene (since acquired by BMS)	Juno therapeutics	$9 billion
Gilead	Kite Pharma	$11.9 billion
Roche	Sparks Therapeutics	$4.8 billion
Novartis	AveXis	$8.7 billion
AbbVie	Voyager Therapeutics	$1.5 billion
Biogen	Nightstar Therapeutics	$800 million
Pfizer	Bamboo Therapeutics	$600 million
Bayer	BlueRock Therapeutics	$240 million

Some specific needs and challenges

- Small batches
  - Flexible filling equipment
  - RTU components
  - traceability
- Cold storage
  - Gene Therapy : -20°C / -80°C (mechanical freezer)
  - Cell Therapy : -180°C (liquid nitrogen)
- High value drugs
  - Pre-qualified packaging solution to reduce risk (development and manufacturing)
  - CCIT : major challenge (rubber undergo glass transition around -60/-70°C)

ARaymondlife and SCHOTT Pharmaceutical Packaging: A joint effort towards a pre-validated solution

Objectives:

- Evaluate the performance of RayDyLyo press-fit caps vs aluminum cap at -80°C
- Demonstrate the ISO glass vial suitability for storage until -80°C
- Propose a pre-qualified packaging solution for gene therapy product storage

SCHOTT Glass Vial, Rubber stopper & RayDyLyo® cap

Value of using a plastic press-fit cap and an ISO standard glass vial

« Ensuring CCI over the product shelf-life including storage, shipment, and intended use is **one of the most critical aspect** in the development and commercialization of parenteral products » (1)

« Several minor or cosmetic defects associated with the capping process, which do not necessary lead to leakages and CCI failure, are responsible for the **majority of rejections and recalls in commercial manufacturing** » (1)

« The integrity of the packaging system is a **complex interplay** of the vial, rubber stopper and crimp cap, but also the capping process (e.g. equipment, choice of parameters and ranges) » (1)

(1) The pharmaceutical vial capping process: container closure systems, capping equipment, regulatory framework, and seal quality tests – Roman Matheas et al. – European Journal of Pharmaceutics and Biopharmaceutics 99 (2016).

Testing Methodology

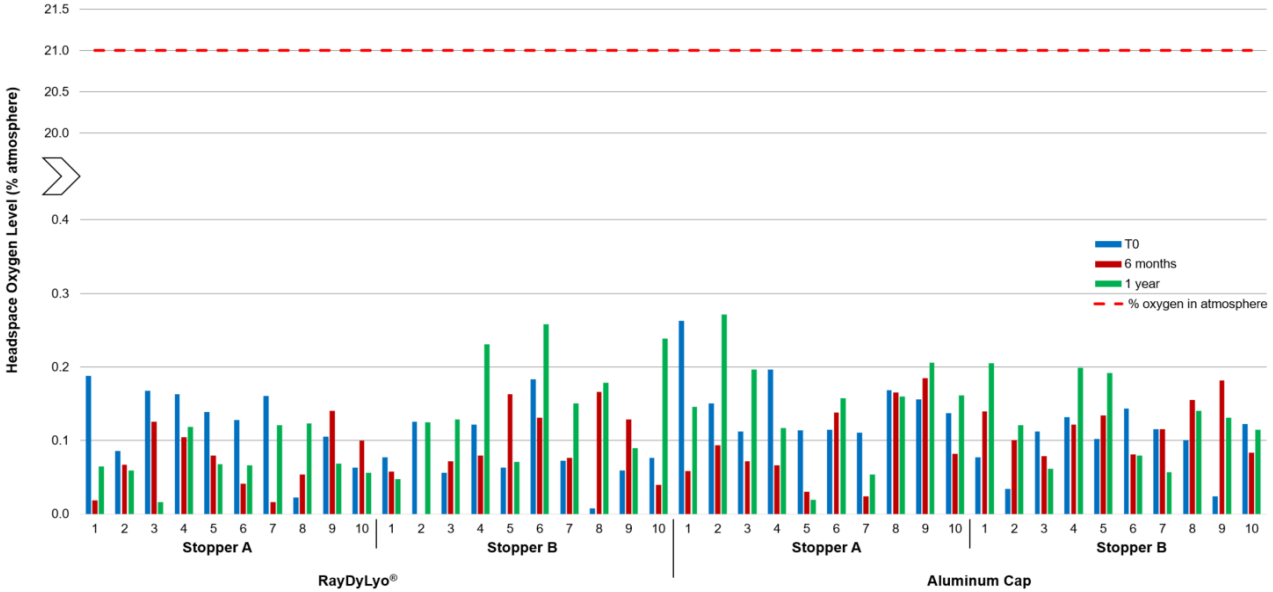
- USP <1207.1> : Package integrity and test method selection to ensure
  - Liquid leakage must be blocked
  - Headspace gas or pressure must be preserved
  - Microbial ingress must be prevented

- Method selection : Frequency modulated tunable diode laser absorption spectroscopy (Lighthouse)
  - None destructive : same samples can be tested at different time points
  - Commonly used and available
  - Capable of detecting leakage when stored at -80°C (sample history maintained)

- Tests performed
  - O_2 ingress measured in the headspace of the vial at room temperature (RT)
  - T_0, T=6 months, T=1 year, T=2 years data.

Results: **13 mm** vial and caps

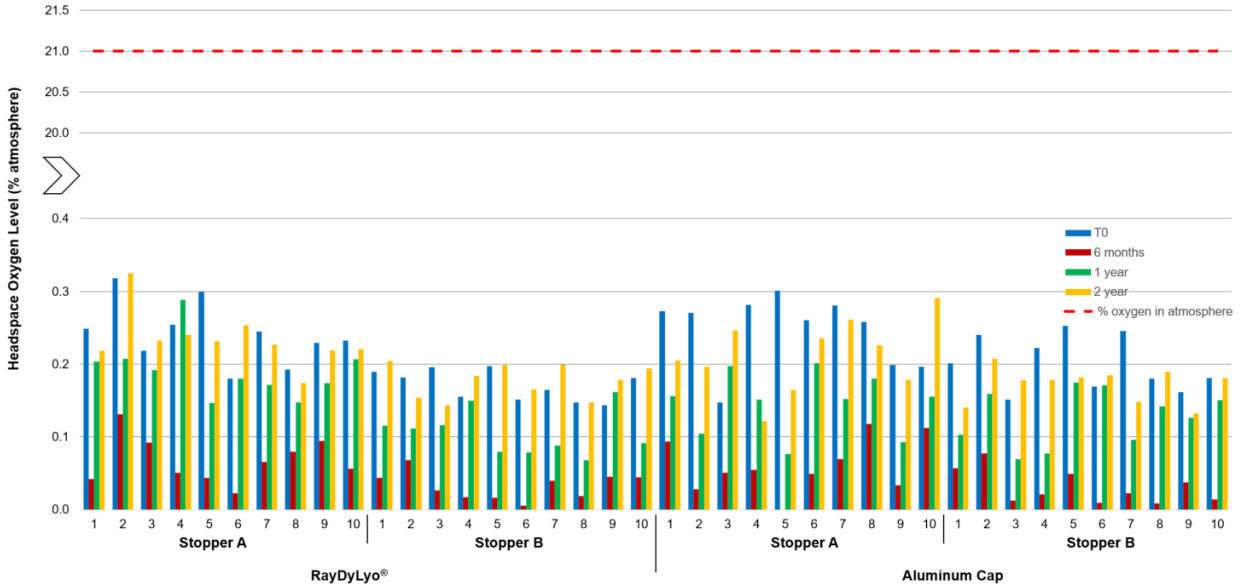
HSA method at RT



- No **significant ingress** of oxygen (<0.2% atm) at T_0, T_1 and T_2
- CCIT maintained with SCHOTT ISO NBB glass vials 13 mm neck and ARaymondlife RayDyLyo® at -80°C for 2 years

Results: **20 mm** vial and caps

HSA method at RT



- No **significant ingress** of oxygen (<0.2% atm) at T_0, T_1 and T_2
- CCIT maintained with SCHOTT ISO NBB glass vials 20 mm neck and ARaymondlife RayDyLyo® at -80°C for 2 years

Conclusions

- Selecting a pre-validated system for the packaging of gene therapy products is ensuring faster time-to-market and patient safety.
- SCHOTT ISO glass vials (2R and 6R) and ARaymondlife RayDyLyo® press-fit caps have been demonstrated to offer a suitable solution for storage of gene therapy products at -80°C (2R and 6R format).
- ARaymondlife RayDyLyo® press-fit cap ensures consistent CCI over 2 years while providing a superior alternative to aluminum caps for RTU usage.

ARaymondlife and Schott vials press-fit cap system are available in RTU for various machine configurations

Bulk Vials / Bagged RayDyLyo®

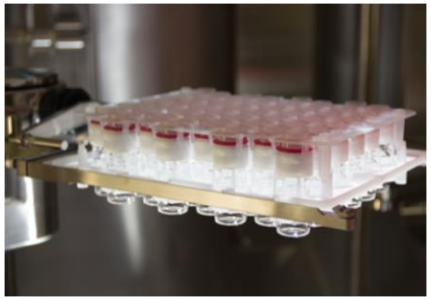
SX-310-RDL
Dara Pharmaceutical Packaging

Nested Vials / Bagged RayDyLyo®

NFL-RDL
Dara Pharmaceutical Packaging

Flexfill
groninger

Nested Vials / Nested RayDyLyo®



Vanrx SA25 and Microcell
Aseptic Filling Workcell

RTU is providing higher patient safety, better scalability and enhancing flexibility

SCHOTT adaptiQ® RTU vials from 2R to 50 vials

Availability of nested RayDyLyo caps

Vial size	Nest format	Caps/Nest	Caps/Tub
2/4R	Nest 13/100	100	300
6/8/10/15R	Nest 20/48	48	144
20/25/30R	Nest 20/25	25	75
50R	Nest 20/16	16	48

ARaymondlife and SCHOTT Pharmaceutical Packaging: A joint effort towards a pre-validated solution

- ARaymondlife and SCHOTT Pharmaceutical Packaging are committed to work together on cryogenic storage challenges and interact with interested customers to address their specific needs and to support validation of customized packaging solutions.

- **We are pleased to further discuss with you at our booths**

Thank you!