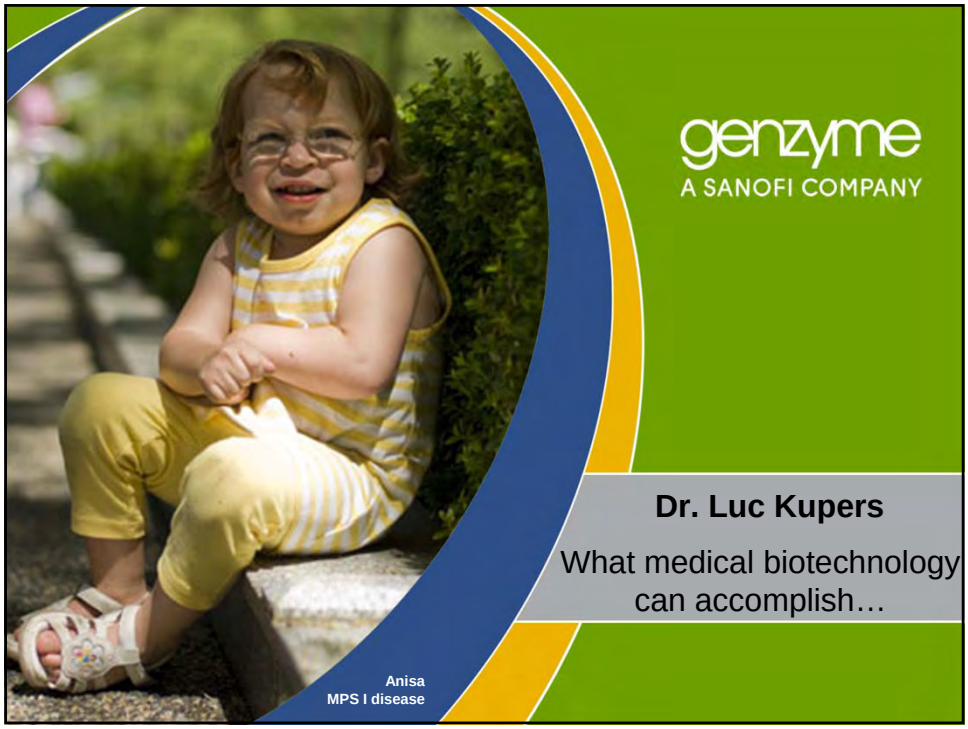

genzyme
A SANOFI COMPANY
Dr. Luc Kupers
What medical biotechnology can accomplish…
Anisa
MPS I disease


Our mission is to discover and deliver transformative therapies for patients with rare and special unmet medical needs, providing hope where there was none before.
genzyme
A SANOFI COMPANY
Rina Gaucher disease Kosov
genzyme
A SANOFI COMPANY
1

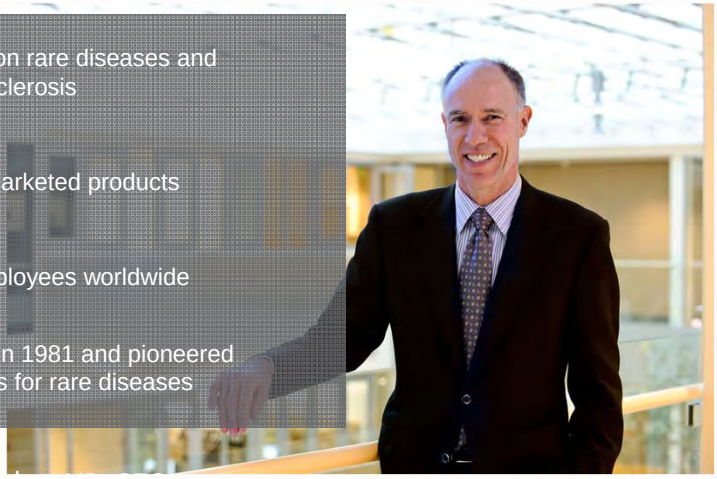
About Genzyme

Focused on rare diseases and multiple sclerosis

7 major marketed products

8,000 employees worldwide

Founded in 1981 and pioneered treatments for rare diseases



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2

A lifetime commitment

"My mom was just tremendous and an amazing role model for me. I know the doctors told her that I was going to die but her perseverance, dedication and ability to work closely with Genzyme and search around the world to develop a treatment was amazing."

– Brian Berman, Type 1 Gaucher disease

1991

2001

2011

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3

Rare diseases / Orphan Drugs

- Orphan drugs are for diagnosis, prevention or treatment of diseases that are **both** rare **and** life-threatening or chronically debilitating
- Without incentives / support, there would be insufficient return on investment for companies to develop such treatments
- Close to 7,000 described rare diseases
- Collectively, these disorders affect 6–7% of the population in the developed world
- Less than 10% of patients afflicted with rare diseases are treated today, and the unmet medical need remains high
- Over 80% of rare diseases are genetic in origin

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The Orphan Drug legislation

- Made a societal commitment: **"patients suffering from rare conditions should be entitled to the same quality of treatment as other patients"**
- Defined which diseases / drugs deserve special treatment
  - RARITY is not enough
  - Needs to be life-threatening or chronically debilitating
  - And no satisfactory existing treatment / new one offers "significant benefit"
- According to EU Regulation:
  - Rare disease = disease with **5 patients/ 10.000 inhabitants** (250 000 in EU)
- According to the US Regulation:
  - Rare disease = less than 200 000
- **Ultra-orphan drugs**
  - Products for conditions with a prevalence of **less than 1 in 50.000**

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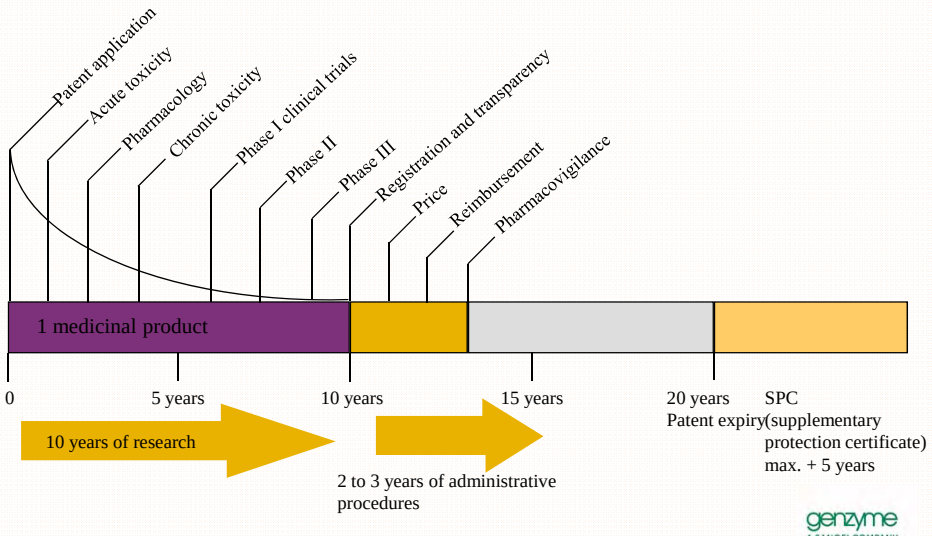
5

Orphan drugs are no different: each must prove they are safe & that they work



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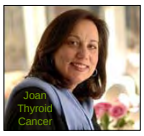
6

Rare Diseases

TREATMENT AREAS

Genetic Diseases

Type1Gaucher disease, Fabry disease, Pompe disease, MPS I disease



Endocrinology

Facilitating thyroid cancer treatment and testing

Cardiovascular

Homozygous Familial Hypercholesterolemia (HoFH)

UNDER REGULATORY REVIEW

Eliglustat Tartrate
for type 1 Gaucher disease

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7

Multiple Sclerosis

One once-daily oral therapy for relapsing MS

UNDER REGULATORY REVIEW

Alemtuzumab
for relapsing multiple sclerosis

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8

Biologics Manufacturing Network

Allston Landing, Boston, MA
Bulk Biologics

Framingham, MA
Bulk Biologics

Geel, Belgium
Bulk Biologics

Waterford, Ireland
Solid Oral Dosage, Fill & Finish

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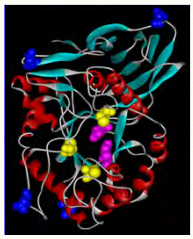
9

Biopharmaceuticals

- have large molecular weights, high structural complexity
- are heterogeneous in terms of molecular species
- are heterogeneous in terms of impurity profile
- are sensitive to physical conditions
- are depending on starting materials, master cell banks or expression systems;
- Post-translational modifications

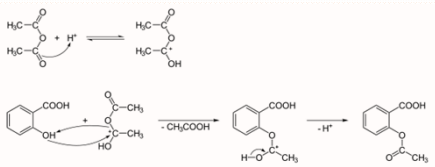


Glycosylation

- Correct folding
- Potency
- Effector functions/Receptor binding
- Immunogenicity
- Pharmacokinetics
- Stability

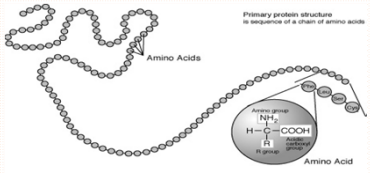
A chemical compound

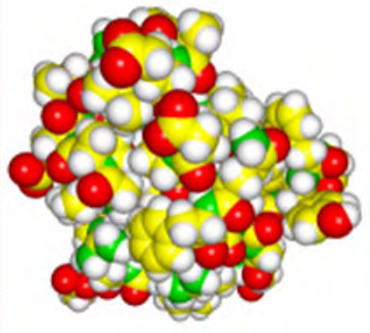
- Aspirin production is a chemical reaction



A protein

- A protein is a chain of amino acids.





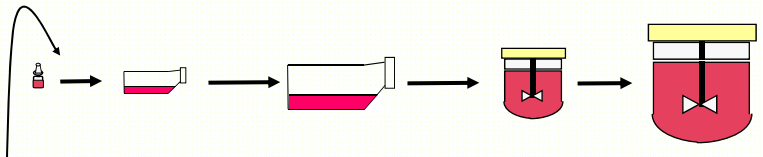
alglucosidase alfa

Genetic defect in the cell: Pompe disease

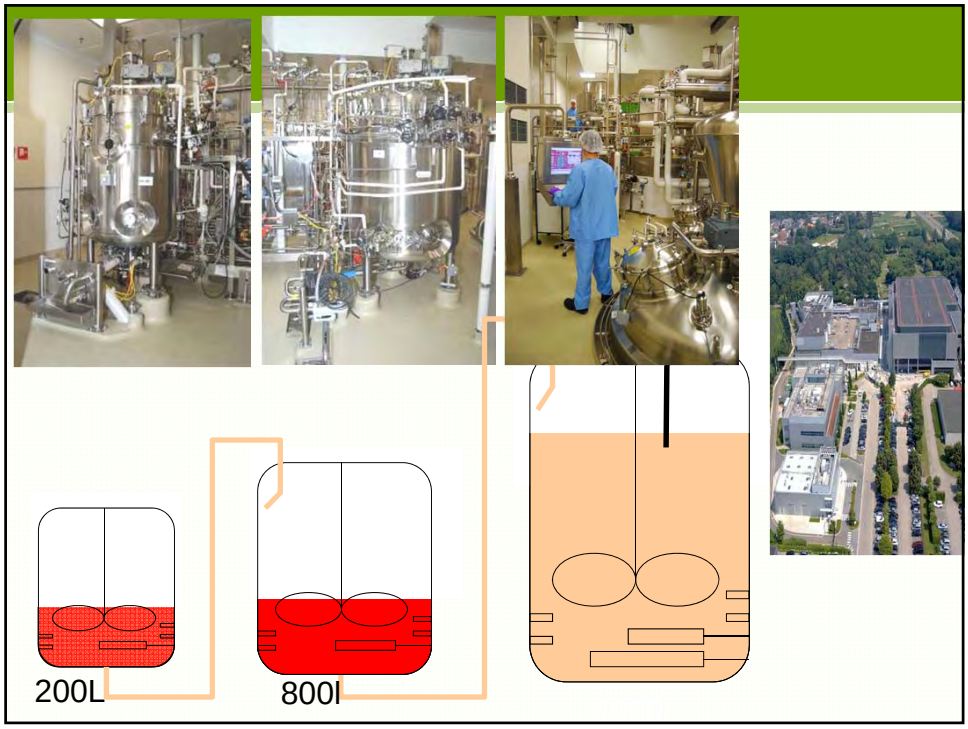
- **Pompe Disease is a debilitating, progressive life-threatening genetic rare muscle disease**
  - Symptoms include: severe muscle degeneration, progressive respiratory failure
- **Cause: genetic defect protein, α-glucosidase, resulting in accumulation of glycogen in muscles**
- **Broad spectrum of clinical symptoms:**
  - Early progressive form (EOPD); baby dies without treatment in first year
  - Late progressive form (LOPD): after the age of 1 year (infants, children, adults)

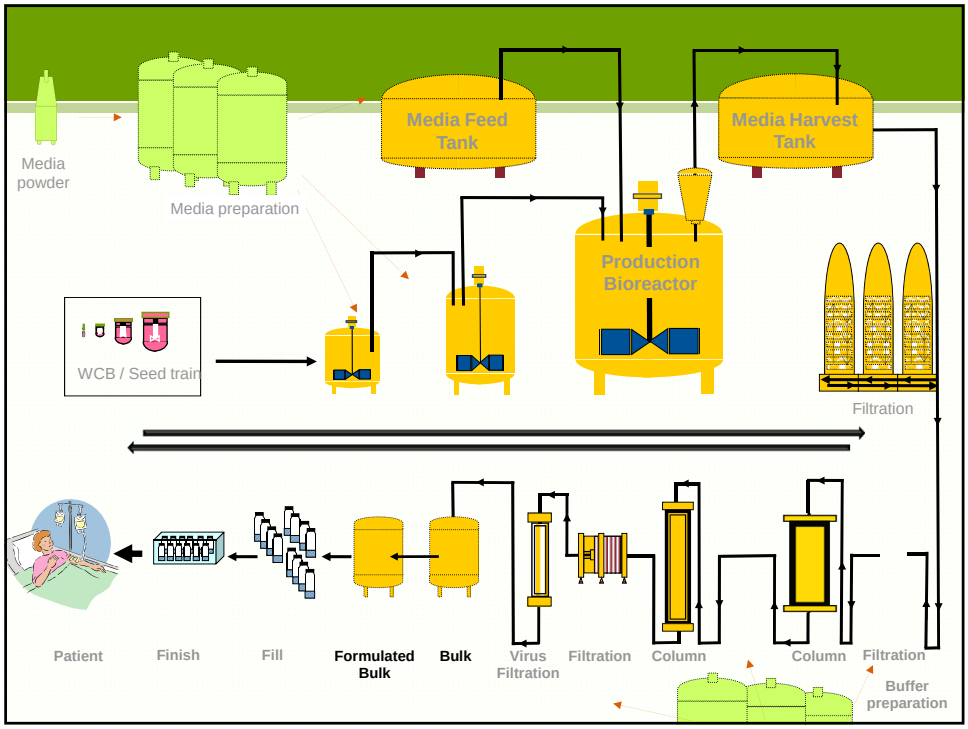
12

Seed train



1 ml	•1 ml + 9 ml GM •Growth for 3 days •10 millions cells	•10 ml + 90 ml GM •Growth for 3 days •100 millions cells	•100 ml + 900 ml •Growth for 3 days •1 billion cells	•1 L + 9 L •Growth for 3 days •10 billion cells

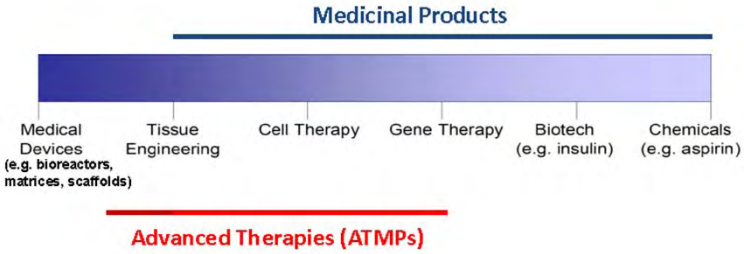

200L
800l


Media
powder
Media preparation
Media Feed
Tank
Media Harvest
Tank
Production
Bioreactor
WCB / Seed train
Filtration
Patient
Finish
Fill
Formulated
Bulk
Bulk
Virus
Filtration
Filtration
Column
Column
Filtration
Buffer
preparation

Our Personalized Approach

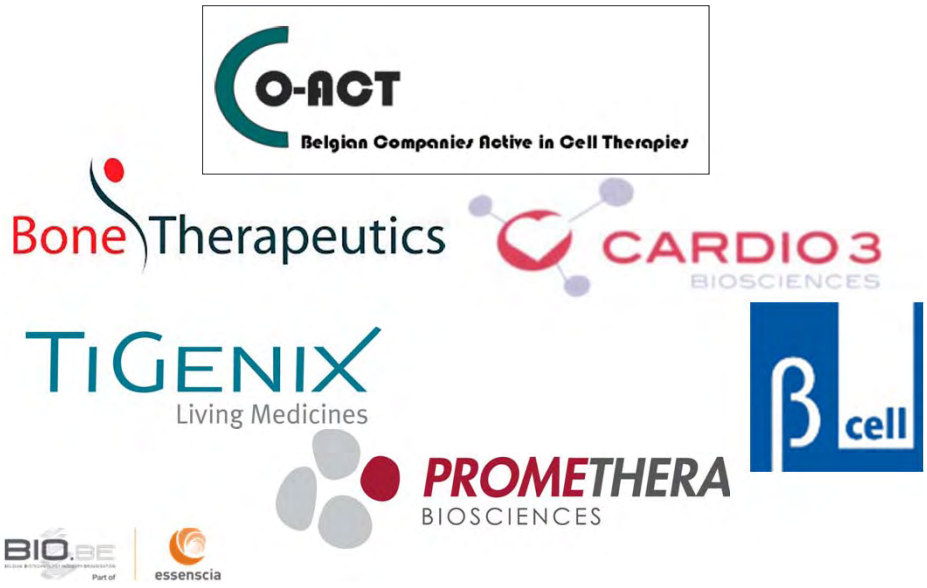
- Strong relationships with patients and patient communities
- World-class research targeted for unmet medical needs
- Compassionate and committed employees

Regenerative medicine with ATMP



- Is just at the beginning of its journey
- Has in it the promise to make the step from treatment to cure, also for old unmet medical needs

ATMP in Belgium

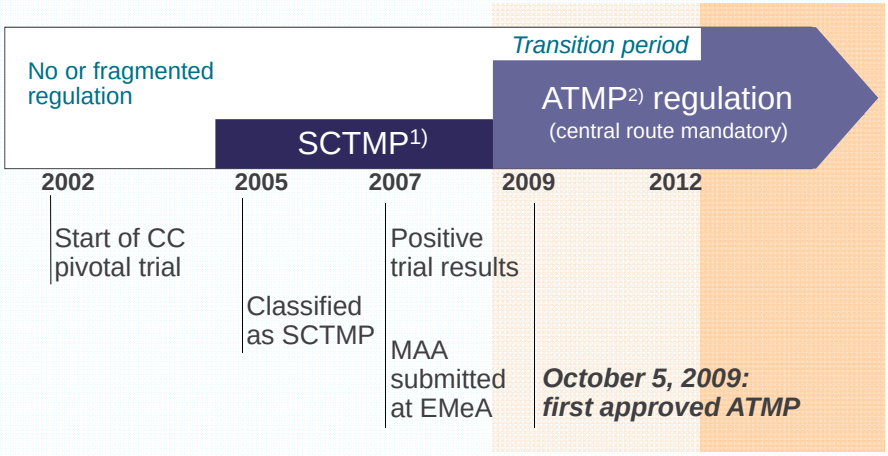


TiGenix

- Founded in 2000, spin-off of Universities of Leuven and Gent (B)
- Listed on NYSE Euronext Brussels and Merged with Cellerix SA in 2011
- European leader in cell therapy – Living medicines
- ChondroCelect, autologous cell-based product for cartilage repair, first and only approved cell-base product in Europe (ATMP)

TiGENIX Living Medicines With permission from Tigenix BIO.BE essenscia

TiGenix



1) Somatic Cell Therapy Medicinal Product
2) Advanced Therapy Medicinal Product

With permission from Tigenix

ATMP in Belgium

- Regulatory framework in place: medicinal product
  - Specific challenges, but it can be done
  - Correct implementation is condition for the field to develop
  - Hospital exemption
  - Cell & Tissue legislation: autologous vs allogeneic
  - Being the only country introducing exclusive obligation to cooperate with hospital based tissue banks
- The work does not stop at regulatory approval…
  - The market access & reimbursement hurdle is high
  - Need for harmonization