



## **GMP Pilot Plant**

Specialized in the production  
of nanopharmaceuticals

June, 12<sup>th</sup> 2019

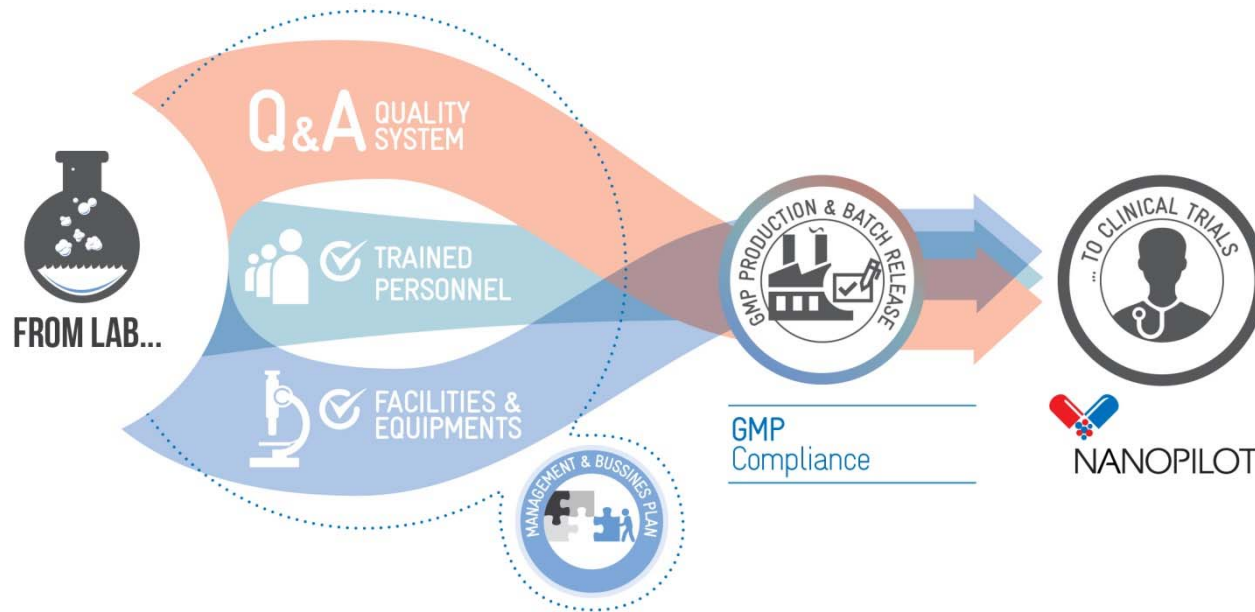
**Iraida Loinaz**

Director of CIDETEC Nanomedicine



# The Aim

NanoPilot has **set-up a flexible and adaptable pilot plant operating under GMP** for the production of **small batches of polymer based nanopharmaceuticals**, which exhibit significant potential in the field of drug-delivery particularly for the design of second generation nanopharmaceuticals.



# NanoPilot



## NANOPILOT

Funded under European Union  
Framework Programme for  
Research and Innovation  
Horizon 2020 under Grant  
Agreement 646142

Project acronym: NanoPilot  
Grant Agreement no: 646142  
Start Date: January 1<sup>st</sup>, 2015  
End Date: June 30<sup>st</sup>, 2019  
Project Budget: 6.28 M Euro  
Type: Research and Innovation  
Action



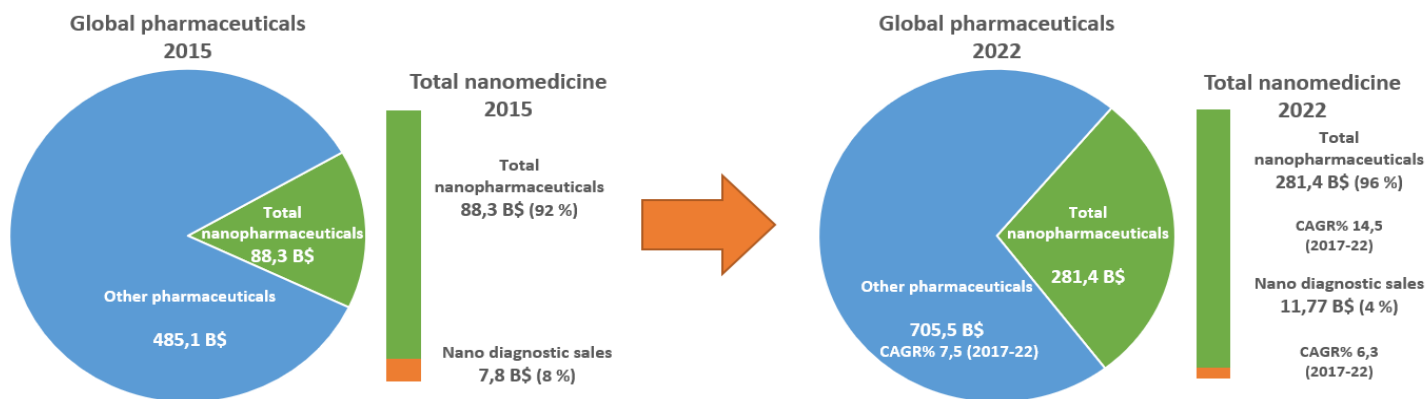
**NanoPilot is a four-year and a half long project** which objective is **to set-up a pilot plant operating under GMP** (Good Manufacturing Practices) for the production of polymer-based nanopharmaceuticals.

Pilot plant's ambition is to accelerate the development of nanomedicine, currently in its infancy within the pharmaceutical sector.

**4 research groups, 3 SMEs and 2 industries**, all of them with significant track record in knowledge creation and innovation in their respective domains of expertise, have joined forces in NanoPilot to guarantee the successful outcome of the proposed project

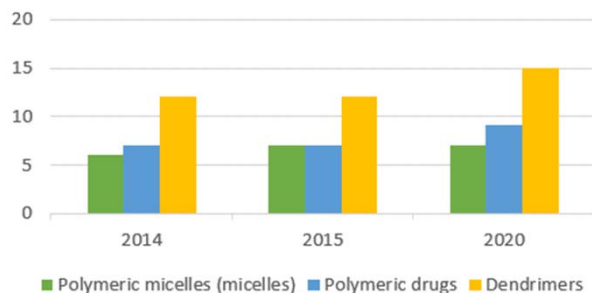


# The Market



Global nanomedicine market, by segment, through 2022 (B\$/%)

Global polymeric therapeutics market in advanced drug delivery by type, 2014-2022 (\$ billions)



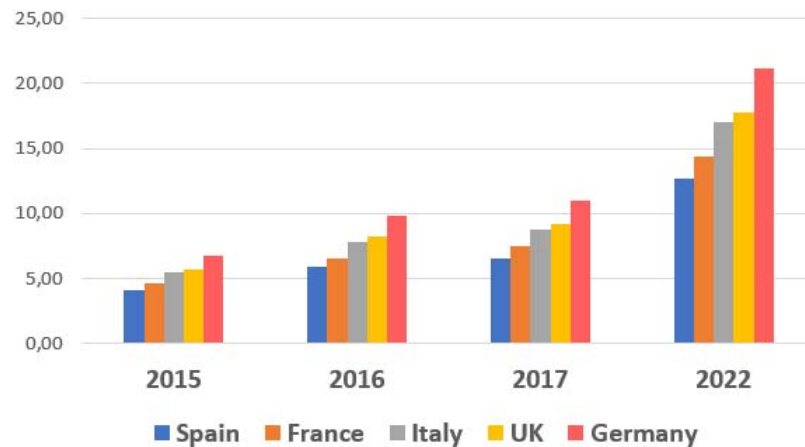
Global polymeric therapeutics market in advanced drug delivery by type, 2014-2022 (B\$)



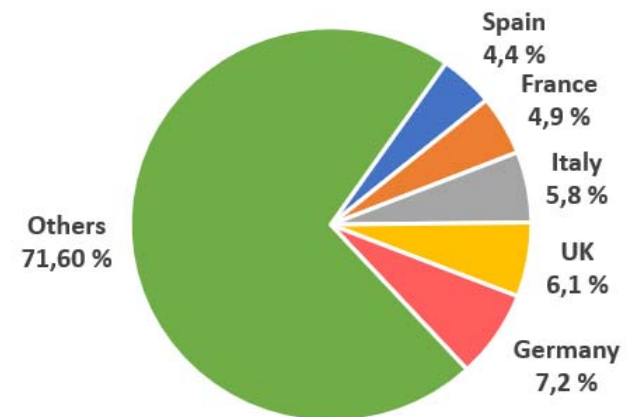


# The Market

**5 largest European nanomedicine markets, 2015-2022 (\$ billions)**



**Global nanomedicine market 2017**



Nanomedicine market of 5 largest European markets 2015-2022, (B\$ and %)

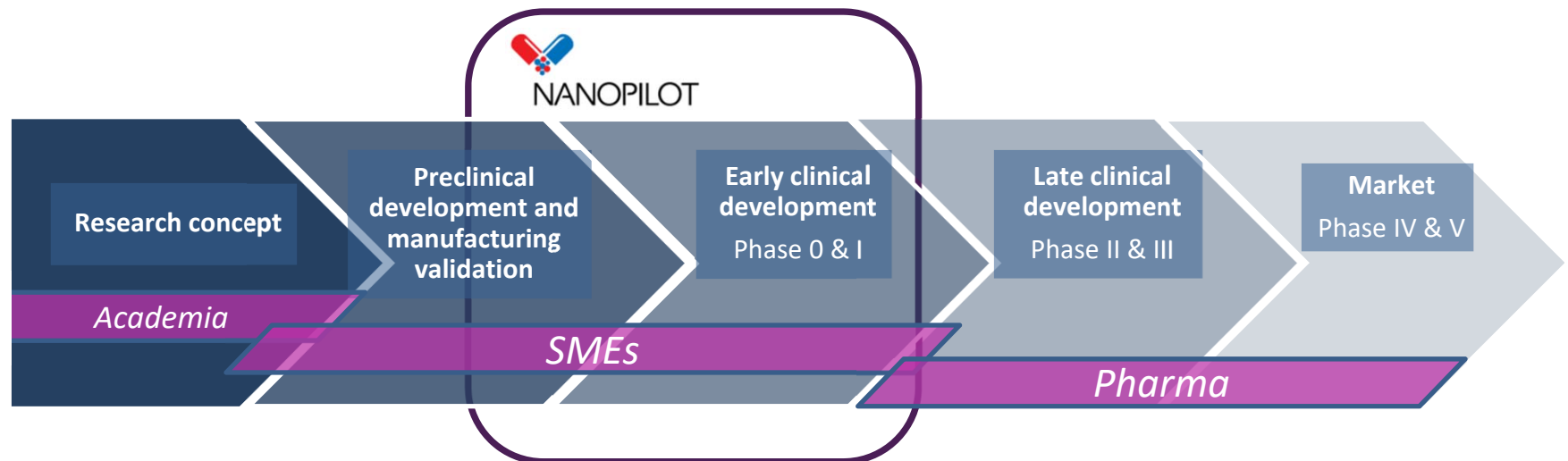




# The Problem

The production of innovative nanopharmaceuticals in quantity and quality (GMP) required for SMEs to enter clinical trials remains a challenge:

- **Medium size companies** with limited R&D facilities, use their existing manufacturing plants, which are too big and too busy for R&D purposes.
- **Small companies** lack of resources to up-scale and implement GMP manufacturing.



# Production of three different nanopharmaceuticals

A treatment for interstitial cystitis/painful bladder syndrome (IC/PBS).



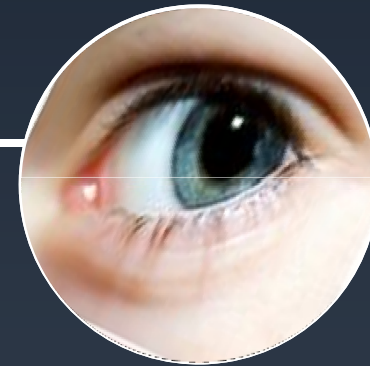
**Hyaluronan based particles**

A HIV nanovaccine formulated for intranasal vaccination



**Peptidic antigens**

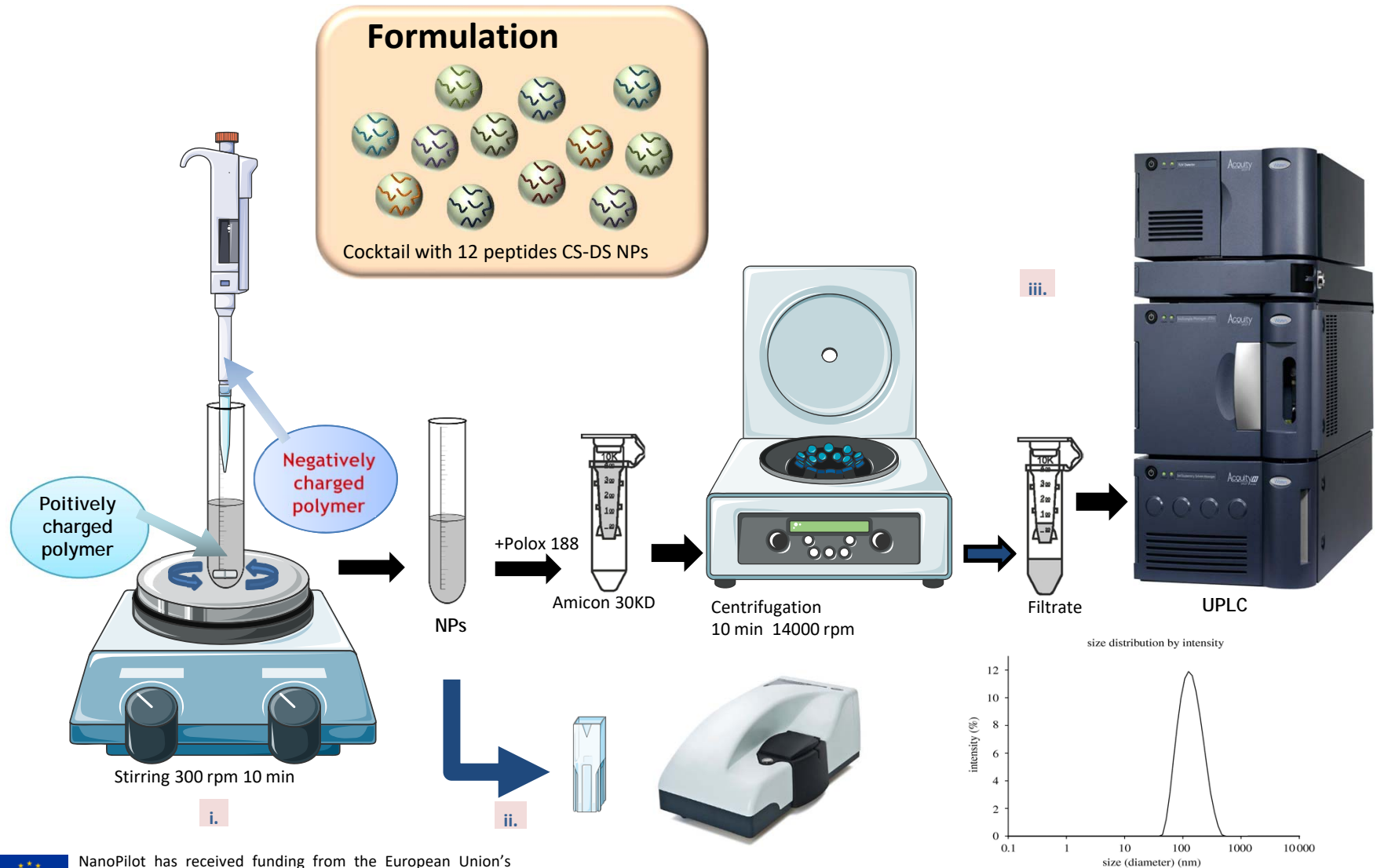
Topical treatment of ocular pain associated with dry eye syndrome (DES).



**A short interfering RNA (siRNA) nanoformulation**



# HIV Vaccine for intranasal vaccination







# HIV Vaccine for intranasal vaccination

- ✓ **QC developed** – complicated to determine how the peptide was anchored to the nanosystems.
- ✓ **Product under preclinical development** to reduce the number of antigens.
- ✓ **USC have shown that reducing drastically the number of peptides they still have a considerable protection in macaques (80 vs 50%, respectively)**

| Characteristic                         | Specification                | Result                       |
|----------------------------------------|------------------------------|------------------------------|
| Identity PCS5-68-1% w/w Retention Time | 4.6 - 5.2 min                | 4.9 min                      |
| Osmolality                             | 100 - 200 mOsm/Kg            | 186 mOsm/Kg                  |
| PDI                                    | <0.3                         | 0.13 ± 0.02                  |
| pH                                     | 5.0 - 7.5                    | 6.6                          |
| Recovery (%) HPLC-UV                   | 90.0 - 110.0 %               | 103.3 %                      |
| RT for Redispersion                    | <10.0 s                      | <10.0 s                      |
| Residual Moisture                      | <5.0 %                       | 2.4 %                        |
| Size                                   | 90 - 200 nm                  | 150.3 ± 0.7 nm               |
| Stat_Size_Distr D(Span)                | 0.4 - 3.0                    | 1.2                          |
| Stat_Size_Distr D(10)                  | 80 - 150 nm                  | 99.9 ± 4.0 nm                |
| Stat_Size_Distr D(50)                  | 150 - 250 nm                 | 163.0 ± 2.1 nm               |
| Stat_Size_Distr D(90)                  | 250 - 450 nm                 | 268.0 ± 16.7 nm              |
| Transmittancy at 236nm                 | <10.0 %                      | 7.2 %                        |
| Uniformity of Dosage                   | ≤ 15.0                       | 13.8                         |
| Visual Appearance                      | White/off-White lyophilisate | White/off-White lyophilisate |
| Z Potential                            | -65.0 - -30.0 mV             | -41.8 ± 0.6 mV               |

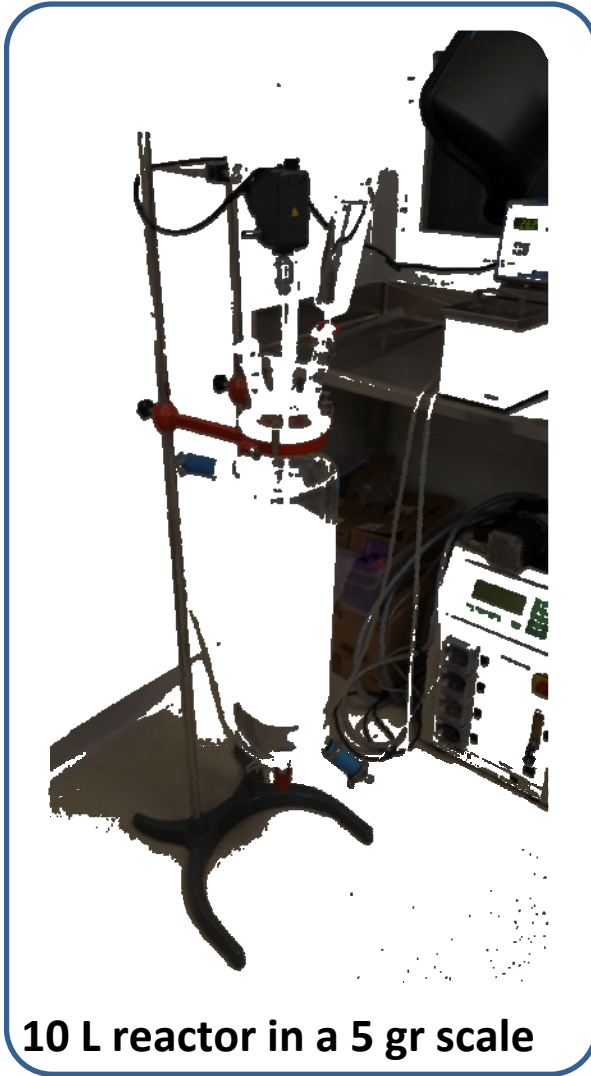


**216 vials batch  
109 sent to USC**



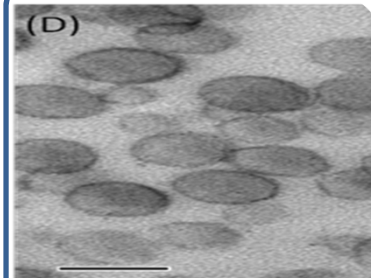


# Hyaluronan particles for interstitial cystitis



**10 L reactor in a 5 gr scale**

- ✓ The manufacturing method was improved.
- ✓ QC developed.
- ✓ The process scaled-up to 5 gr.
- ✓ Sterilization method was developed (gamma irradiation).
- ✓ Partner NUIG is engage with a Company Aspire and has licenced the technology.
- ✓ Two patent applications filed.

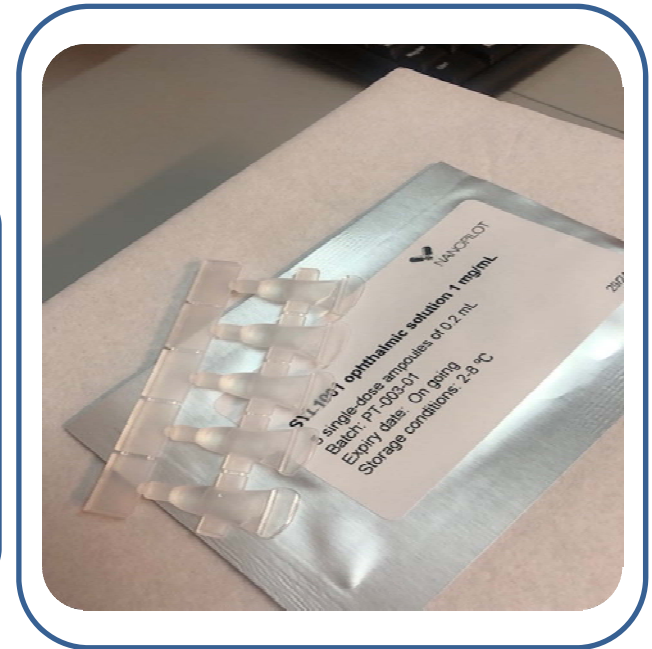


**280 vials batch  
25 vials for QC and  
255 sent to NUIG**





# Ophthalmological formulation of siRNA



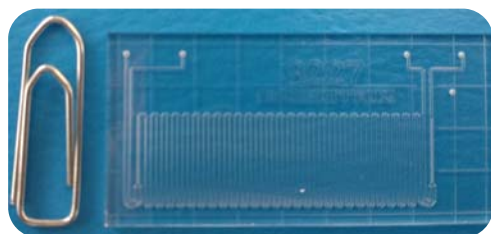
- ✓ The nanoformulated siRNA was not stable and the polydispersion of the particles was too low.
- ✓ Non-nanoformulated siRNA was manufactured successfully in aseptic conditions.
- ✓ 1200 single-dose ampoules (240 strips) were manufactured.
- ✓ This product is in Phase III at the moment.



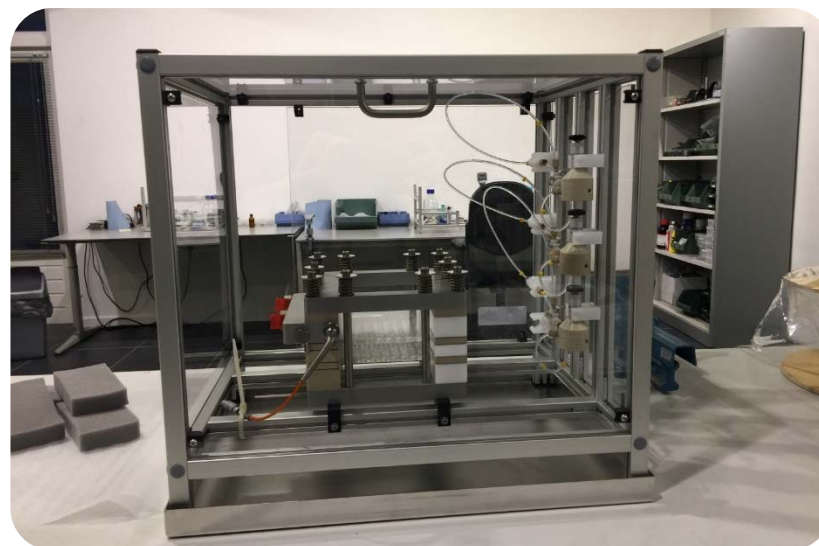


# Continuous flow reactors

*From lab scale...*



*...to pilot.*



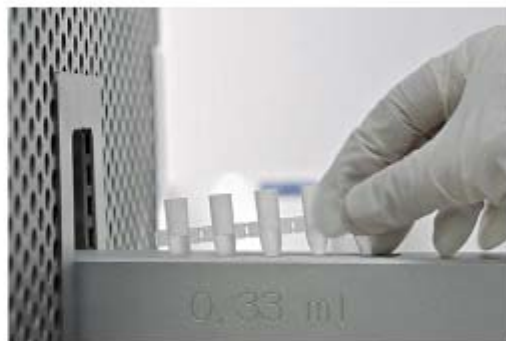


# The Plant





# Services



## Specialized service in technology transfer:

- Customized service.
- Definition of specifications.
- Reproducibility and technology evaluation.
- Definition of critical process parameters.
- Characterisation (polymer science and nanotechnology).
- Development of lyophilisation processes.
- Scaling-up.

## Production Capacities of investigational medicinal products:

### Lyophilizates: up to 600 vials/7,5 mL

- Non-sterile lyophilizates.
- Sterile lyophilizates

### Liquids:

- Non-sterile liquid formulations
- Monodosis (500-100 strips batches)





# Value Proposition

**Highly specialized** on polymer chemistry and nanotechnology

**Flexible to the customer needs:** Multi-product plant.

**Highly qualified R&D team** to support the development of innovative projects.

**Cost-effective:** Includes small equipment to produce only required amount of doses.

**Dedicated to technology transfer from lab to pilot scale** – Unlike CMOs which are interested in the production of big batches.

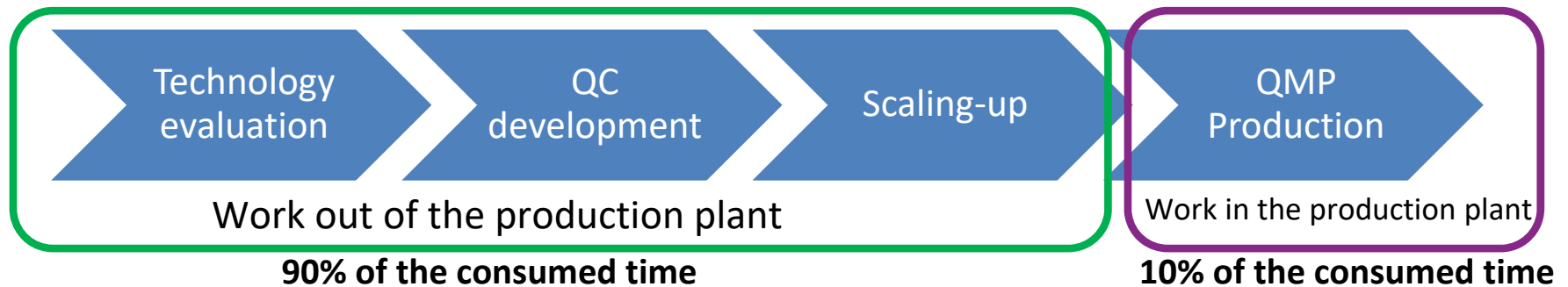




# Business Plan

## Market demand

- ✓ Nanopharmaceutical market is still unmaturred:
  - ✓ Demand needs to grow yet
  - ✓ Products under development still in early development stages, not in the target of the GMP Nanopharmaceutical plant yet.
    - ✓ Typical situation of the case studies developed in NanoPilot:



- ✓ Same situation in 4 spin off companies we have been working with: they need to scale up process before GMP manufacturing.





# Business Plan

## Feasibility study

- ✓ **With actual expected demand and previewed operational costs of the plant, the business is not sustainable.**
- ✓ **More resources are required to take the plant to the break even point, which is expected to happen in 2022.**



# Business Plan: Strategy

## 1. Increase the short term demand for the plant:

- Include the production of other investigational medicinal products not necessarily based on nanotechnologies.
- Include commercial products requiring continuous production of small batch size (i.e. orphan drugs, products with limited shelf life, etc.).

## 2. Increase capabilities of the plant in the near future:

- New capabilities to produce commercial nanopharmaceuticals and investigational nanopharmaceutical products that wouldn't require a large batch sizes.
- Automatization of aseptic filling etc.
- Increase quality control capabilities

## 3. Get external funds and reduce risk in the CIDETEC:

- Open the plant for external investors
- Spin out the activity of the plant from CIDETEC so that enables a better framework for external funding and risk taking in the development of the activity. Also necessary to produce commercial drugs.



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# Business Plan

## Activities

Under this new strategy, several activities have been tackled:

- ✓ **Contacts with partners and investors.**
- ✓ New activities including the manufacturing of other pharmaceutical products, synergic with the nanopharmaceuticals (10 possible commercial products have been selected).
- ✓ **Legal analysis to spin out the plant.**
- ✓ Boost development **proprietary nanoplatform** for the design of new nanopharmaceuticals including the production in the plant.



Dr. Iraida Loinaz  
iloinaz@cidetec.es

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nanomedicine

a greater future today