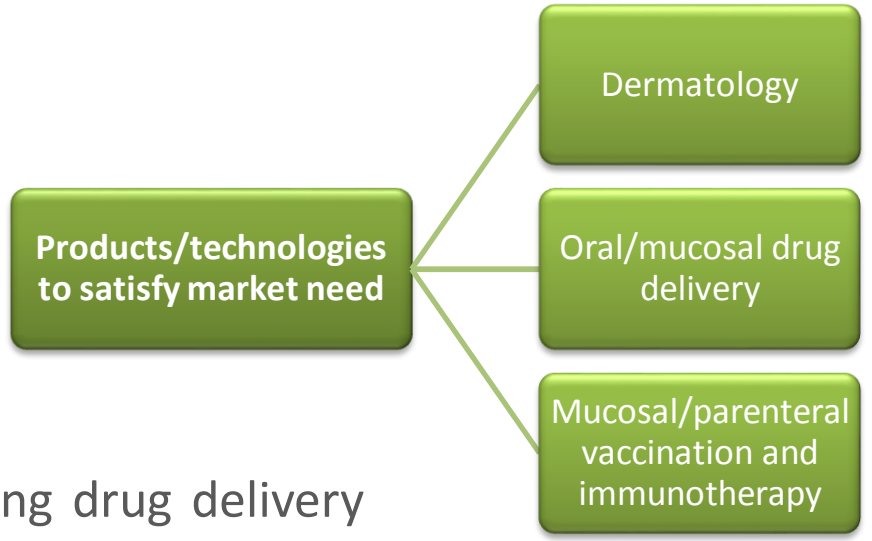
BIONANOPLUS
DRUG DELIVERY TECHNOLOGIES

Real nanotechnology solutions for drug delivery problems

A Drug Delivery Company

Bionanoplus is a drug delivery company focused on the development of technologies and products for different market niches.



Innovation

Bionanoplus efforts have been focused on solving drug delivery problems based **on three patented technologies.**

More than 15 years experience

In house Pharmaceutical development (Drugs and vaccine)

- Design, development and evaluation bioadhesive drug delivery systems (Nanoparticles, nanocapsules, nanoemulsion, microemulsion, in situ-self assembled nanoparticles)
- Industrial scale and final dosage from design.
- *In vitro* or *Ex vivo* evaluation and efficacy prediction

Certified as compliant with the principles of GLP

Key milestones achieved

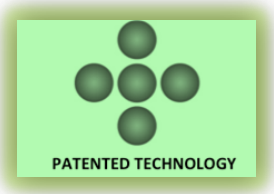
Own products

- ❑ One product approved for the Spanish regulatory agency.
  - Indication: hair loss.
  - Commercialization expected for Q3 2016
- ❑ PoC clinical trial planned for 2017
  - Indication: oral lichen planus
- ❑ Other 6 products are ready for licensing or co-development

Products developed for third-party

- ❑ Two PoC clinical trials planned for Q3 2016 and 2017
  - Indications: undisclosed
- ❑ One marketed product in the veterinary field
  - Indication: mucosal vaccine against rainbow trout infection

Intellectual property



Our Patents are the basic value for our own products and R&D services

- ❑ Easy manufacturing and scale up
- ❑ GRAS listed and cheap raw materials

IP 1: Topical adhesive technology: Intellectual property rights until 2032-3

PCT/EP2012/056900: Nanoparticles comprising esters of poly (methyl vinyl ether-co-maleic anhydride) and uses thereof

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IP2: SANP technology: Intellectual property rights until 2032-3

PCT/EP2013/052795: Nanoparticles comprising a vegetable hydrophobic protein and a water miscible non-volatile organic solvent and uses thereof

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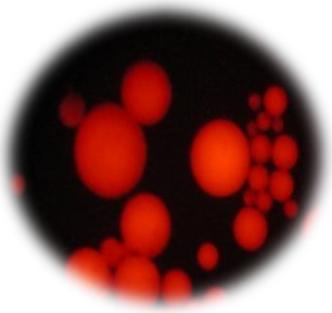
IP3: MUCO-LAST technology: Intellectual property rights until 2036:EP16382136

Business model

In house R&D Services

- Preformulation design
- Design, optimization and characterization of polymeric particulate systems
- Evaluation and analysis of dosage from
- Map design of industrial scale and technology transfer
- Evaluation in Franz Diffusion Cells using different types of tissue (Pig or human skin)
- Evaluation of nail permeation and efficacy assay by microbiological tests



Own Products

- Hair loss
- Psoriasis
- Onychomycosis
- Oral lichen planus
- Oral Aphthous ulceration
- Actinic Queratosis

- Physico-chemical tests (galenic, stability and physico-chemical)
- Pharmacokinetics (including Franz cell studies)
- Analytical and bioanalytical test (HPLC-DAD, HPLC-FLD, UV-V)

BIONANOPLUS
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In house R&D Services and Capacity

Our Experience

Bionanoplus is a drug delivery company specialized in providing innovative technologies and formulation solutions **for topical (skin, nail), buccal, Oral, esophageal, vaginal delivery**

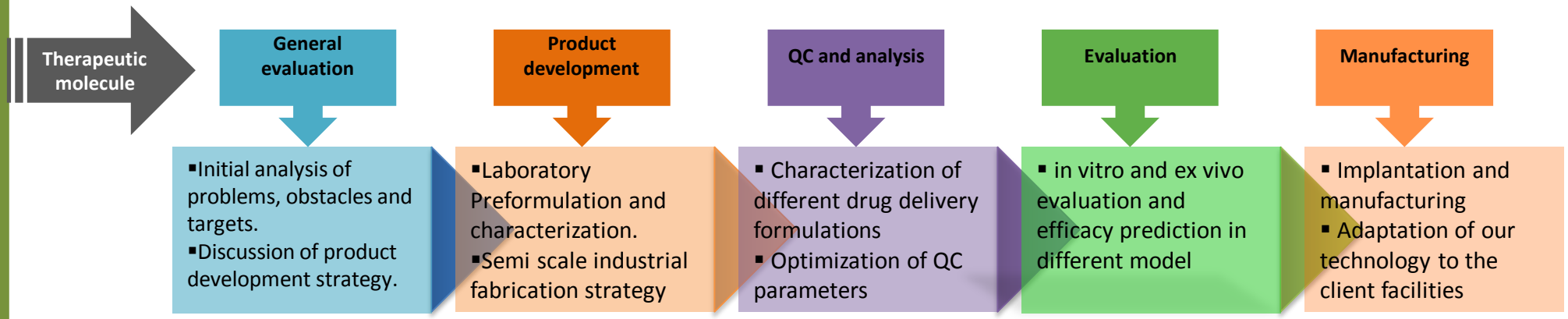
In house Pharmaceutical development (Drugs and vaccine formulations)

- ❑ Design, development and evaluation of bioadhesive drug delivery nanosystems for different routs of administration
- ❑ *In vitro* and *ex vivo* models for evaluation and efficacy prediction
- ❑ Optimization of manufacturing methods, final dosage from design and technology transfer

R&D services

Topical and mucosal drug delivery unit

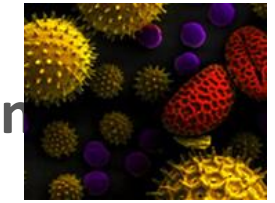
- **General evaluation. Preformulation design**: Drug solubility and general physicochemical properties
- **Product development:** Design, optimization of drug-loaded formulations based on different **polymeric technology platforms** (Compatibility studies, formulation design, stability studies, characterization, etc)
- **QC and analysis:** particle/droplet size, Z-potential, encapsulation efficacy/drug distribution, total drug content (HPLC-DAD, HPLC-FLD, UV-V), pH, viscosity, Osmolarity, etc.
- **Evaluation:** (Franz Diffusion Cells, Nail permeation studies and microbiological efficacy assay, Evaluation of mucoadhesion in different mucosal surfaces: *in house* models*)*
- **Manufacturing and Industrial scale:** Optimization of manufacturing methods and technology transfer

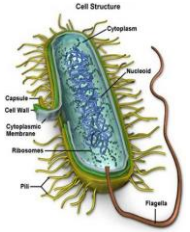


R&D services

Immunoadjuvant Unit (Veterinary and human vaccine polymeric adjuvants

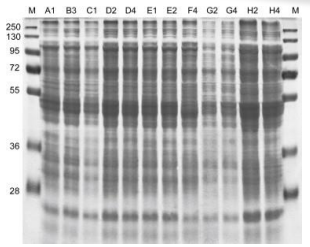
- Design of antigen extraction methods from the target microorganism
- Encapsulation of the antigens with the mucoadhesive technology that increases the mucosal vaccination efficacy
- Adjuvant design: Sub-unit vaccine based on polymeric systems that adapted to client needs achieves the efficacy target through a specific route of administration (Oral, nasal, sublingual and buccal vaccination)
- Design and evaluation of subunit vaccines and immunoassays (Electrophoresis, ELISA, W. BLOTT, etc)
- Vaccine stability assays
- Design and optimization of QC parameters and industrial scale

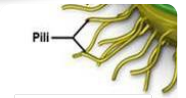


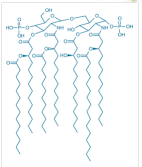


✓ Optimization of Extraction method of target antigen from pathogens or allergic source

✓ Characterization, SDS- page, W. blott



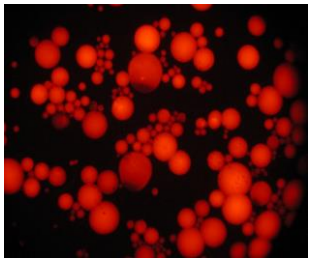


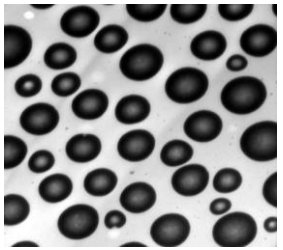


Antigens: Proteins, LPS.etc

✓ Polymeric Adjuvant design: Association of antigens with Bionanoplus polymeric systems

✓ Characterization and assay





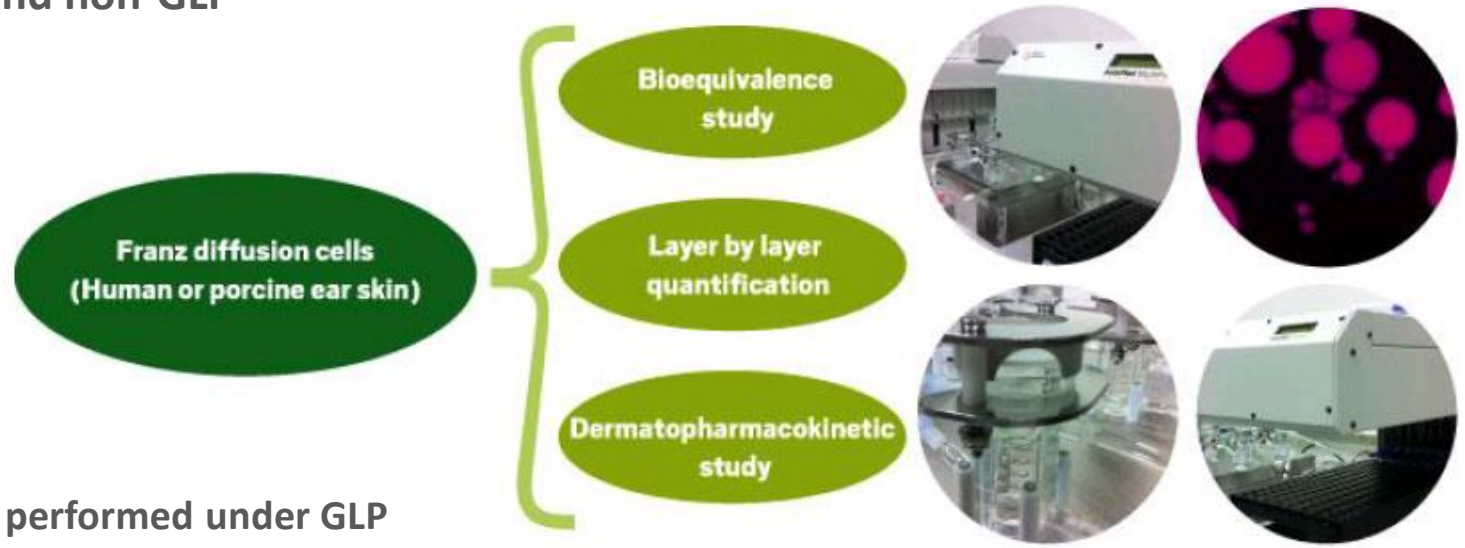
R&D services: In vitro Skin PK studies

Franz Diffusion Cells studies

Bionanoplus provides an adequate dermatopharmacokinetic evaluation of actives in human or pig ear skin under standardized parameters using Franz Diffusion Cells according to ICH guidelines. **Bionanoplus has performed more than 20 studies under both GLP and non-GLP conditions.**

More than 5 years expercince

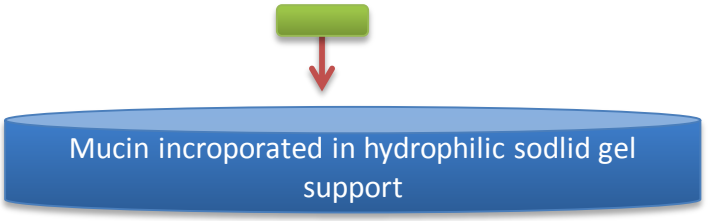
- ❑ Skin dermatomization
- ❑ Skin thickness measurement
- ❑ Skin integrity measurement (TEWL)
- ❑ Permeation study
- ❑ Tape stripping technique
- ❑ Skin layers separation (stratum corneum, epidermis and dermis)



All Franz Cell studies can be performed under GLP

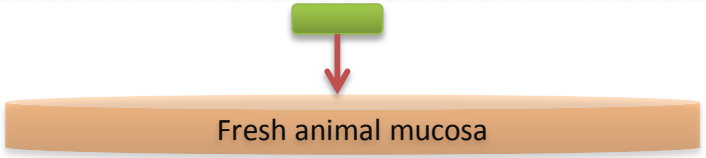
R&D services: Other *in vitro* model studies

In house developed models



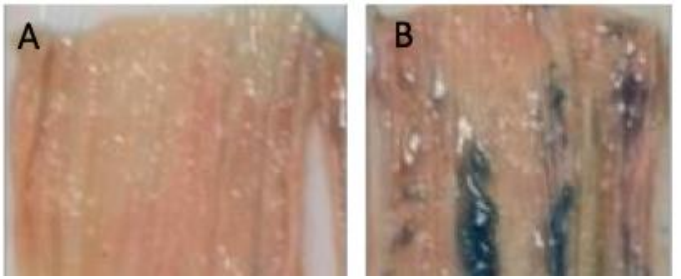
❑ ***In vitro*** **mucosal adhesion (mucine gel support disc)**

- Assay of adhesion kinetics
- Assay of drug release profile (colorimetric, fluorescence techniques)



❑ ***Ex vivo*** **buccal mucosal adhesion (Bovine, porcine buccal mucosa)**

- Assay of adhesion kinetics
- Assay of drug release profile (colorimetric, fluorescence techniques)
- Assay of drug permeation



❑ ***Ex vivo*** **oesophageal adhesion in *Ex vivo* adhesion study in horse esophagus**

- Assay of adhesion kinetics
- Assay of drug release profile (colorimetric, fluorescence techniques)
- Assay of drug permeation

R&D services: Other *in vitro* model studies

In house developed models

❑ *In vitro* nail permeation/efficacy system (Bovine nail disc technology)

Nail discs can be obtained with different thickness, weight and size suitable for a wide variety of assays conditions.

Based in TurChub ® assay (a modified Franz cell), Bionanoplus has developed the **CES** methodology that combine two different and **complementary** *in vitro* tests to evaluate the efficacy of onychomicosis topical treatment. This system allows:

- Measurement of **both antifungal activities**: Inhibition and fungicidal activities
- High conditions **versatility** to get closed to real dosage regimen (treatment duration, doses frequency…)
- **High throughput screening** of formulations

Bovine hooves

Procesing

Nail discs

- ❑ **Nail permeation assay**
- ❑ **Inhibition-permeation system (IPS):** Fungal inhibition after the treatment
- ❑ **Block agar system (BAS):** Fungicidal after the treatment

Contact Detalis

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LET US HELP YOU IN...

- Increasing bioavailability of hydrophobic or hydrophilic molecules
- Improving stability
- Increasing drug solubility
- PK modification
- Controlled releasing of molecules
- Enhancing of residence time
- Drug targeting
- Drug isolation from incompatible excipients