The ART of making peptides
**LIPOTEC GROUP**

**BCN Peptides** is the group’s fine chemical division focused entirely to the cGMP manufacture of Bioactive Peptides.

**GP Pharm** is an independent company with industrial / financial investors that operates in the R&D, manufacturing and commercializing of new products for pharmaceutical business based on Drug Delivery Systems.

**Lipotec** being the first of the companies founded in 1989 deals with the encapsulation of cosmetic actives and the production of novel actives in Cosmetic field.

**Diverdrugs** is a research company participated by the group which is specialized in the field of Drug Discovery through combinatorial libraries and rationale design approaches.

**Lipofoods** is a joint venture with industrial investors dedicated to the encapsulation of actives for the Food Ingredient Industry including the development and production of Novel Foods.

**Prima-Derm** is the company into the group that is selling Finished Cosmetic Products (SingulaDerm®) into the market through Pharmacy channel.
Quality, Experience and Flexibility in GMP Bulk Peptides
We concentrate our efforts on the following activities:

- **Generic Peptides**
- **Custom Synthesis** of proprietary API Peptides

**BCN Peptides** is completely focused on the cGMP manufacture of Bioactive Peptides for Pharmaceutical and Veterinary applications.
We are the **Experts** in the Solid Phase Synthesis of **Bioactive API Peptides**

**Key Technologies**

- Solid Phase Synthesis
- **HPLC** Purification
- Lyophilisation under **GMP** Conditions
- Sterile grade Peptides
BCN Peptides works under the highest Quality Standards for strongly regulated markets. Our activities always follow strict GMP Compliance.

We have been granted with six CEP’s from the European Pharmacopoeia for the following products:

- Salmon Calcitonin (Sterile grade)
- Leuprolide (Sterile grade)
- Somatostatin
- Desmopressin
- Goserelin
- Buserelin
BCN Peptides works under the highest Quality Standards for strongly regulated markets. Our activities always follow strict GMP Compliance.

**BCN Peptides** has been inspected and approved by:

- US FDA
- EDQM
- Different National Authorities Worldwide
- Several Top Ten Major Pharmaceutical Companies

NEW **BCN Peptides** has been authorised (March 2010) to work as Pharmaceutical Laboratory for the analysis of **pharmaceutical final product.**
BCN Peptides' range of activities:

- **Analytical Development**
  - Characterization
  - Working Standard Preparation
  - Establishment of Specifications
  - Analytical Methods set up and Validation

- **Synthetic Development**
  - R&D (Route development)
  - Scaling up
  - Validation Batches
  - Process Validation

- **ICH Stability Study**
- **CTD/DMF preparation**
- **Regulatory Support in front of US FDA / EMEA**
- **Commercial Manufacturing**
- **Analysis of pharmaceutical final product**
Collaboration with:
European Pharmacopoeia

2001  Collaboration in the preparation of the monograph of Goserelin
       Collaborative study Protirelin

2002  Collaborative study Tetracosactide, Salmon Calcitonin and Leuprorelin

2003  Collaborative study Ferlipressin and Gonadorelin.

2004  Supply of bulk of Salmon Calcitonin
       Collaborative study Protirelin (CRS3)

2005  Study of the impurity profile of the standard Tetracosactide.

2006  Collaborative study Buserelin

2007  Monograph review for the product Tetracosactide
       Request of changes in the monograph of Goserelin
       Supply of bulk of Somatostatin

2008  Collaborative study of Goserelin, Oxitocin, Tetracosactide and Somatostatin

2010  Supply of impurities of Buserelin and batches of Buserelin
Collaboration with: USP Pharmacopoeia

2005  Bulk supply of *Gonadorelin Diacetate*, *Gonadorelin Hydrochloride* and *impurity A*.

2008  Collaborative study of *Vasopressin*.

2010  Supply bulk of *Vasopresin* and Collaborative study of *Vasopressin*. Supply bulk of *Desmopressin*

2011  Collaborative study *Octreotide*
Looking for an **API Peptide**?

<table>
<thead>
<tr>
<th>Product List</th>
<th>BCN Peptides</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Growth Hormone Regulators</strong></td>
<td><strong>Secretins</strong></td>
</tr>
<tr>
<td>Octreotide</td>
<td>Synthetic Human Secretin</td>
</tr>
<tr>
<td>Somatostatin</td>
<td>Synthetic Porcine Secretin</td>
</tr>
<tr>
<td>Vapreotide</td>
<td></td>
</tr>
<tr>
<td><strong>Calcium Regulating Hormones</strong></td>
<td><strong>Thymus Hormones</strong></td>
</tr>
<tr>
<td>Elcatonin (Carbocalciton)</td>
<td>Thymosin alpha 1</td>
</tr>
<tr>
<td>Salmon Calcitonin</td>
<td>Thymosin beta 4</td>
</tr>
<tr>
<td><strong>LHRH Analogue Agonists</strong></td>
<td><strong>Miscellaneous</strong></td>
</tr>
<tr>
<td>Buserelin</td>
<td>Carbetocin</td>
</tr>
<tr>
<td>Fertirelin</td>
<td>Eledoisin</td>
</tr>
<tr>
<td>Gonadorelin</td>
<td>Glucagon</td>
</tr>
<tr>
<td>Goserelin</td>
<td>Protirelin</td>
</tr>
<tr>
<td>Leuprolide</td>
<td>Tetracosactide</td>
</tr>
<tr>
<td>Triptorelin</td>
<td>Teniparatide (pTH I-34)</td>
</tr>
<tr>
<td></td>
<td>Vasoactive Intestinal Peptide</td>
</tr>
<tr>
<td><strong>Vasopressin Analogues</strong></td>
<td></td>
</tr>
</tbody>
</table>
BCN Peptides can manufacture **multi kg** batches of GMP Peptides using Solid Phase Synthesis technology.
Facility plan: Offices and Laboratories
Facility plan: Flow of material and personnel
The ART of making peptides
GP Pharm

Innovative Drug Delivery Systems in Urology and Oncology
GP Pharm is a Spanish biopharmaceutical company, founded in 2000 and located in Gavà (Barcelona – Spain).

The company is specialized in research, development, manufacturing and marketing of products for injection within Oncology and Urology fields, based on own innovative drug delivery systems.

These technological platforms include Microspheres and Liposomes.

The company works in the complete development of these drugs, from the preclinical studies until the launch to the market.

GP Pharm is commercially international oriented, supplying its products through either owned net sales forces or strong alliances with partners.

The company doubled its turn-over in 2010 and reached in 2011: 13,6M€, maintaining its constant investment in R&D.

The company has currently 100 employees from which more than 50% are high qualified: either PhDs or Bachelor Degrees.
GP Pharm Activities

**R&D Projects**

- GP Pharm develops Drug Delivery formulations for injection for its own and for third parties, applied to Oncology CNS and CVS.

**Contract Manufacturing**

- GP Pharm is able to produce cyto-toxics and hormonal products in drug delivery platforms for its own and also for third parties, although it is mainly interested in NCE or added value products.

**Licensing In & Out**

- GP Pharm would like to expand its international presence through well-established pharmaceutical companies, in order to promote and distribute its portfolio products with licensing and supply agreement. Also, it is looking for potential partners to co-develop its clinical projects in advanced stage.

**Commercialization**

- GP Pharm has its own commercial structure in Spain and Portugal, and is building up subsidiaries in South Europe countries and South America. Its commercial world-wide strategy is based on licensing, joint ventures, and distribution agreements.
ROYALTIES*
Eg.: STATINS-PUFA
SYRUP-DESMOPRESSINE
PRO-INSULINE

*R+D in other fields (not Cancer or Urology)
Microspheres for sustained release. POLITRATE®.

- GP Pharm has experience obtaining Microspheres through different technologies such as: **double emulsion** and **coacervation**.

- Patented Triethyl Citrate and PLGA Polimer Microspheres.

- Ability to control release from 5-6 days up to 6 months.

- Use of Triethyl Citrate in different ratios within the capsule surface allows to encapsulate virtually any water soluble molecule.

- Non patent infringing, European and US patents for the system have already been awarded.

- Enhanced control during release phase.

- Enhanced sustained release during the whole treatment.

- Enhanced pharmacologic effect.

- Decrease of the requested dose per administration unit.
GP Pharm has expertise using different composition of lipid components for Liposome preparation: cationic, anionic, neutral (being used separately or in different ratios).

Also expertise obtaining Liposomes through out different sizing technologies such as: microfluidification, extrussion and sonication.

- Drug substance included in the wall of the liposome.
- Presence of lipochromann an antioxidant product in the wall of the liposome.
- Reduced drug substance degradation process.

Sarcodoxome® Designation as Orphan Drug. EMEA and FDA, phase II study. (Liposome Doxorubicin)

Target Liposomes: Under development
## Product Portfolio (I)

### Microspheres formulations

<table>
<thead>
<tr>
<th>Product</th>
<th>Phase I</th>
<th>Phase II</th>
<th>Phase III</th>
<th>Registration</th>
<th>Marketing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lutrate® Depot (Leuprolide 1 month)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lutrate® Depot (Leuprolide 3 months)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lutrate® Depot (Leuprolide 6 months)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Risperidone Depot (Risperdal Consta)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Triptorelin 1 and 3 months</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Octreotide Depot</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Minoctre® (Octreotide MAR)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

2nd Generation, LHRH and other hormones
Liposomal formulations

<table>
<thead>
<tr>
<th>Sarcodoxome ® (Liposomal Doxorubicin)</th>
<th>Preclinical</th>
<th>Phase I</th>
<th>Phase II</th>
<th>Phase III</th>
<th>Registration</th>
<th>Marketing</th>
</tr>
</thead>
</table>

Orphan drug status

2nd Generation Cytotoxics

Target Liposomes

<table>
<thead>
<tr>
<th></th>
<th>Preclinical</th>
<th>Phase I</th>
<th>Phase II</th>
<th>Phase III</th>
<th>Registration</th>
<th>Marketing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Doxorubicin</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Irinotecan</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gemcitabine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

3rd Generation, targeting Cytotoxic Delivery
### Hormonal products

<table>
<thead>
<tr>
<th></th>
<th>Pharmaceutical development</th>
<th>Manufacturing development</th>
<th>Registration</th>
<th>Marketing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Octreotide</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Somatostatin</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nictur TM (Desmopressin oral drops)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


**Product Portfolio (IV)**

**Generic Cytotoxics for Injection**

<table>
<thead>
<tr>
<th>Pharmaceutical development</th>
<th>Manufacturing development</th>
<th>Registration</th>
<th>Marketing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxaliplatin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Irinotecan</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gemcitabine</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Some future projects:**

PEG Liposomal Doxorubicin (Caelyx)
Pemetrexed (Alimta)
GP Pharm’s production facility is located in Sant Quintí de Mediona (at about 75 Km from Barcelona) and in a 35,000 square meters area.

The plant consists on 6 isolated buildings and 3 of them are exclusively dedicated to production.
Approvals and Certifications

- GMP approved facilities by EMEA (European), TGA (Australian) and PMDA (Japanese) Authorities

Recently, also approved in Gulf Countries, Canada and Turkey
Contract Manufacturing Services

Which products?

- Sterile drug products for injection of:
  - Finished dosage forms with indications for the treatment of cancer (cyto-toxics).
  - Finished dosage forms of high potency drug substances (hormonal).
  - Drug delivery systems: microspheres and liposomes.

Which dosage forms?

- Vials.
- Ampoules.
- Pre-filled syringes.

Which formulations?

- Liquid.
- Freeze dried.
GP Pharm is allowed to manufacture investigational medicinal product.

Facilities has achieved requirements on annex 13 of eGMP.

Hence our facilities are specially authorized to manufacture products on clinical development.
Warehouse and Services Building

Providing good manufacturing items from the beginning

- Cold-storage rooms, either for stability studies of storage of finished.
- Segregated areas for quarantine, approving and rejection of samples.
- Sampling area.
- Water for pharmaceutical use: purified water (WFI and pure steam are produced in independent loops in each plant to avoid cross contamination).
- Industrial steam and return of condensers.
- Sanitary cold water.
- Sanitary hot water.
- Compressed air.
- Technical gases.
- Natural gas.
1953
DOUBLE HELIX STRUCTURE
(Watson & Crick)

2003
DNA DECODIFICATION
(Human Genome Project)

2008
PERSONALIZED MEDICINE

HOY
PERSONALIZED COSMETICS
“We are all, regardless of race, genetically 99.9% the same”

James D. Watson, HGP’s Director
90% of variation at the genetic level: SNPs
- Not all of the SNPs have effects on health:
  - intergenic regions
  - synonymous SNPs
SNPs determine how prone your skin is to wrinkles, oxidative damage, collagen breakdown, photoaging, etc.

By determining SNPs we are able to know your skin’s overall health and wellness.
- 3.7 millions of SNPs in the genome
- 60,000 of SNPs are in the exons regions
- SNPs sinonimum
- SNPs No-sinonimum
- Biological function in the skin
- 20% of population
- COL1A1   - LOXL1   - ICAM1   - SOD2
- COL3A1   - MUSK    - CRP     - EPHX1
- MMP1     - CHRNA1  - ADCY9   - NQO1
- MMP2     - CHRN1B  - SLC24A5 - GSTT1
- MMP3     - CHRND    - MC1R    - GSTM1
- ELN      - CHRNE    - HSPA1A  - ADIPOQ
- LAMB3    - HYAL1    - FOXO3A  - NOC
- FBLN5    - HYAL2    - GADD45A -

- Tissular Architecture
- Wrinkle
- Sensitive Skin
- Pigmentation
- Longevity
- Slimming
- Detoxification
SNPs profile

Fluorescence-Detection DNA Chip

1. Labeling target DNA with fluorescent dye
2. Attaching the probe DNA to the chip
3. Hybridization and cleaning of target DNA
4. Capturing images with the CCD sensor

Identifying the hybridized probes by image processing
STEP 1
DNA sample & life’s style
STEP 1
DNA sample & life's style
STEP 2
DNA sample & life’s style

Algorithm

HISTORIAL CLÍNICO – ESTILO DE VIDA

<table>
<thead>
<tr>
<th>Estilo de vida</th>
<th>Sí</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ejercicio regular</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Despersonalizada</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Descanso suficiente</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Estrés</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Consumo de tabaco</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Consumo de alcohol</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Consumo suficiente de agua (&gt;31/4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complemento antioxidante</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Bronceado por exposición solar
  - No
  - Por favor, especifique frecuencia....

- Utilización de cabina de bronceado artificial
  - No
  - Por favor, especifique frecuencia....

- Utilización de protector solar
  - No
  - Por favor, especifique SPF....

Medicación y Salud

- Enfermedades
MULTISPECTRAL ANALYSIS OF THE DERMIS AND EPIDERMIS IN 2 AND 3 DIMENSIONS

BY ANTERA3D™

In vivo test with 56 volunteers T=0, T=7, T=14, T=21 days

Dermatological evaluation and supervision of the study

Dr. Noguera
Centro Epidermos, Barcelona- May 2013
VOLUNTEER 110
BOOSTERS

CUTANEOUS INTOLERANCE | HIPERPIGMENTATIONS | CELLS LONGEVITY
Wrinkle overall size

- t = 7: 100%
- t = 14: 72.3%
- t = 21: 57.3%

Wrinkle overall width

- t = 7: 100%
- t = 14: 99.4%
- t = 21: 81.5%
$t = 7$

$t = 14$

$t = 21$
VOLUNTEER 121
BOOSTERS
DERMAL STRUCTURE | WRINKLES | CUTANEOUS INTOLERANCE
VOLUNTEER 126
BOOSTERS
CUTANEOUS INTOLERANCE | CUTANEOUS DETOXIFICATION | CELLS LONGEVITY
Hemoglobin average level

- $t = 7$: 100%
- $t = 14$: 92%
- $t = 21$: 91.1%
VOLUNTEER 123

WRINKLES | HYPERPIGMENTATION | CUTANEOUS INTOLERANCE
Hemoglobin average level

- t = 7: 100%
- t = 21: 84.1%

Wrinkle overall size

- t = 7: 100%
- t = 21: 47.8%

Wrinkle overall depth

- t = 7: 100%
- t = 21: 52.9%

Wrinkle overall width

- t = 7: 100%
- t = 21: 94.5%
TREATMENT + PREVENTION
DISTRIBUTION CHANNEL

DERMAGENE
- 8 SNP’s
- 350€ (approx.)
  - Standard

GENEWISE
- 16 SNP’s
- 250€ (approx.)
  - Supplements + Standard

GENE ME
- 8 SNP’s
- 225€ (approx.)
  - Standard

SKIN DNA
- 15 SNP’s
- 500€ (approx.)
  - Without product

DERMAGENETICS
- 6 SNP’s
- 300€ (approx.)
  - Without product

+ DISTRIBUTION CHANNEL
CLINICAL COSMETOGENOMIC SOLUTION

- ADN analysis
- TAYLOR MADE program
- NUTRICIONAL & LIFE’S STYLE guidelines
- CUSTOMIZED product
UNIQUE cutaneous care program that offers MAXIMUM PERFORMANCE and GUARENTEED SUCCESS.
THE PROGRAM CONSISTS OF:

- A genetic study
- Clinical history and comprehensive skin analysis
- Cutaneous *anti-aging* genetic report
- Personalized cosmetogenomic regimen
- Cutting edge technology
- Only available on doctor’s office
- Different from anything available in market until now
CONTINUARÁ