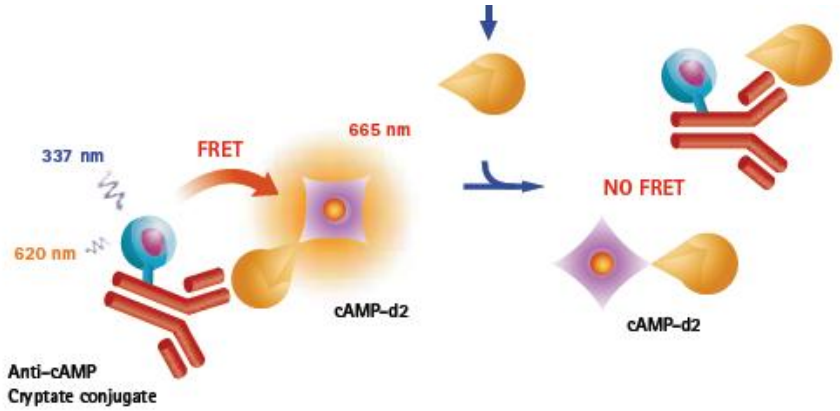
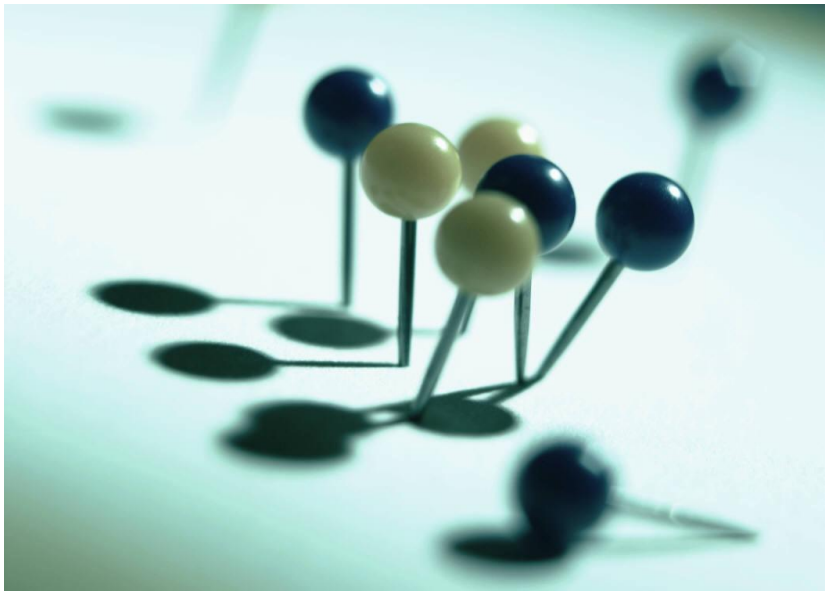
Experience on HTRF technology in public-private collaborations

Brea J, Burgueño J, Dordal, A, Monroy X, Domènech MT, Jover I, Orellana A, Gómez LI, Mascaró C, Loza MI



Agenda

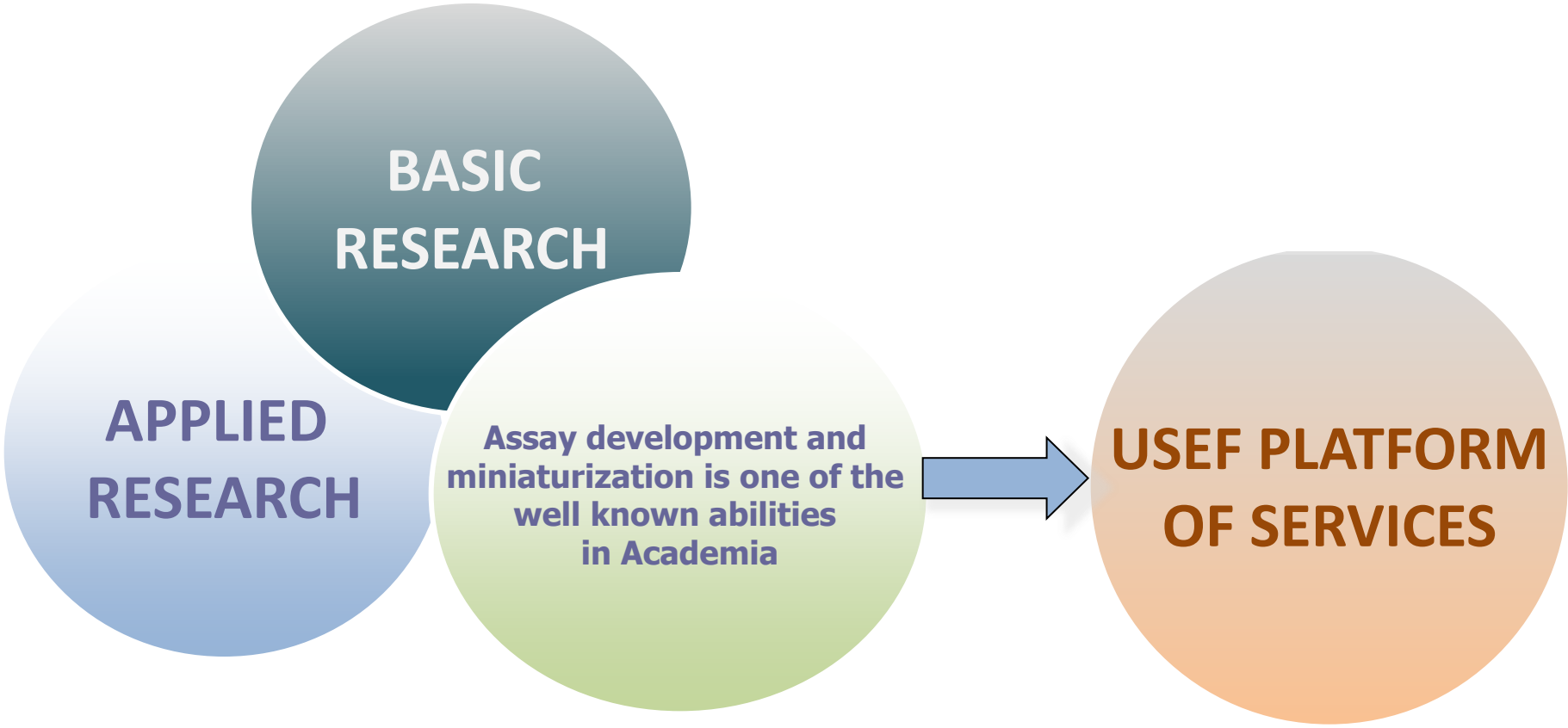
- BioFarma group. University of Santiago de Compostela
- The Neogenius Pharma project
- CisBio HTRF as primary screening



- Multidisciplinary team of **40 professionals** (12 PhDs) with high standards in academic research.
- **More than 100 scientific papers** in international journals in the last five years More than 200 contributions in several international and national meetings.
- **72 competitive research projects** (Galicia, España, EU, NIH).
- Reference group within the academic public sector in Spain in **drug discovery** with more than ten years collaboration with pharmaceutical and biotechnology companies.
- As a result of this research, the **USEF platform** was created as an applied branch of BioFarma in 2004, offering a catalogue of screening services to public and private research groups.

USEF PLATFORM

Neogenius Pharma



OUR EXPERIENCE

1. PHARMACEUTICAL COMPANIES

• The group continually carries out collaborative projects with the two major Spanish pharmaceutical companies: Laboratorios Almirall and Laboratorios Esteve, as well as with another companies (Lacer, Ferrer, Salvat, Draconis).

• USEF participates in 2 CENIT projects (Spanish government initiative for fostering public-private collaborations; the project budget is shared between pharmaceutical companies and the government): Genius Pharma AIE and Neogenius Pharma AIE..

• Open Innovation Joint Units: Esteve implemented a Joint Research Unit within an open innovation environment at the USEF facilities.

• IMI OpenPHACTS project with 14 public groups and 8 pharmaceutical companies (including GSK).

2. BIOTECHNOLOGICAL COMPANIES

• USEF continually carries out collaborative projects with Spanish biotechnological companies (Vivia Biotech, Brainco, Oryzon, Palo Biofarma).

• Biofarma/USEF participates in the CENIT MIND project with the Spanish Biotech company Oryzon Genomics.

•Biofarma/USEF participates in the CENIT DENDRIA project with the Spanish Biotech companies Oryzon Genomics and Brainco Biopharma.

•Biofarma/USEF participates in two INNPACTO projects with Spanish Biotech companies: HUMANFARMA with Vivia Biotech, Vivia Biosystems, Oryzon Genomics and Galchimia, and POLYFARMA Oryzon Genomics and Palo Biofarma.

ACADEMIC GROUPS

- We apply our know-how to the public sector, facilitating **translation** of basic academic research ideas to drug discovery projects, thus adding value to academic projects.

- BioFarma/USEF **collaborates** with public research groups from Spain, Europe (University of Glasgow, University of Cambridge, University of Bari,…), and the US (University of Pittsburgh, University of San Antonio, Scripps Research Center).

- Biofarma/USEF regularly hosts European and US researchers

- EU projects: Currently, Biofarma/USEF participates as a partner in the EU-ADR project and in the Open-PHACTS IMI project. The group is also participating in the preparatory phase of EU-OPENSCREEN project for the ESFRI initiative, together with the Barcelona Science Park.

AVAILABLE TECHNOLOGIES

- Radioactivity (Filtration and SPA)
- Absorbance
- Fluorescence
- Fluorescence polarization
- FRET
- BRET
- Homogeneous Time-Resolved Fluorescence
- Luminiscence
- Alphascreen
- FLIPR
- Automated patch-clamp
- Label free (DMR)
- Lab on a chip
- Luminex
- UPLC/MS

PROGRAMS

Neogenius Pharma

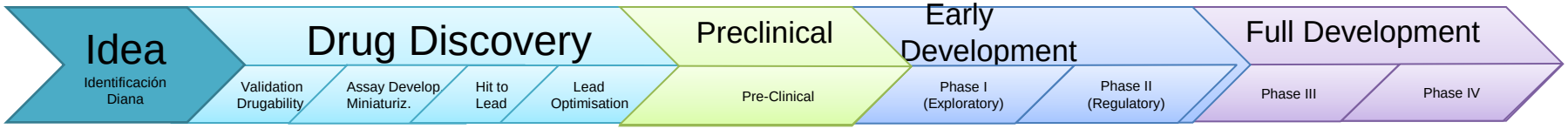
BioFarma

- **ASSAYS SET-UP AND MINIATURIZATION**

- **SCREENING OF CHEMICAL LIBRARIES**
  - Screening of chemical libraries in a target.
  - Selectivity of hits at several targets/antitargets.
  - Functional characterization of compounds at human and animal receptors.

- **SCREENING PACKAGES**
  - *Lead profiling package* (more than 50 studies over different targets/antitargets).
  - ADME-TOX package: cytotoxicity (10 tumoral cell lines available), safety (hERG, Na^{+} and Ca^{+2} channels) and pharmacokinetics (solubility, Caco2, CYP inhibition).

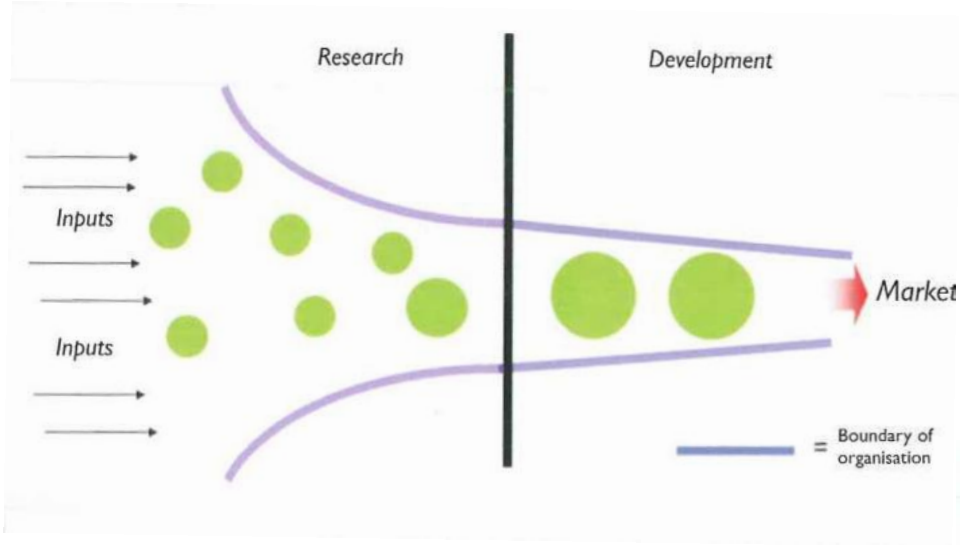
- **FULL EARLY DRUG DISCOVERY PROGRAMS TO PRECLINICAL CANDIDATES, applying translational methodologies**
- **EARLY PROOF OF CONCEPT using predictive biomarkers of response.**



THE NEOGENIUS PHARMA PROJECT

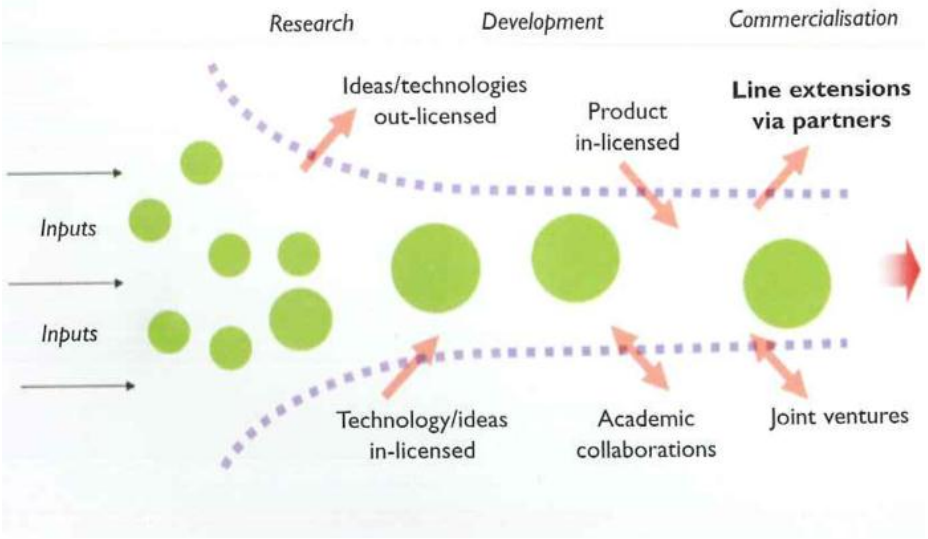
OPEN INNOVATION

Neogenius Pharma



CLOSED innovation model

OPEN innovation model



Is the pharmaceutical industry open for innovation?
Hunter, J., Drug Discov World, fall, 9-14, (2010)

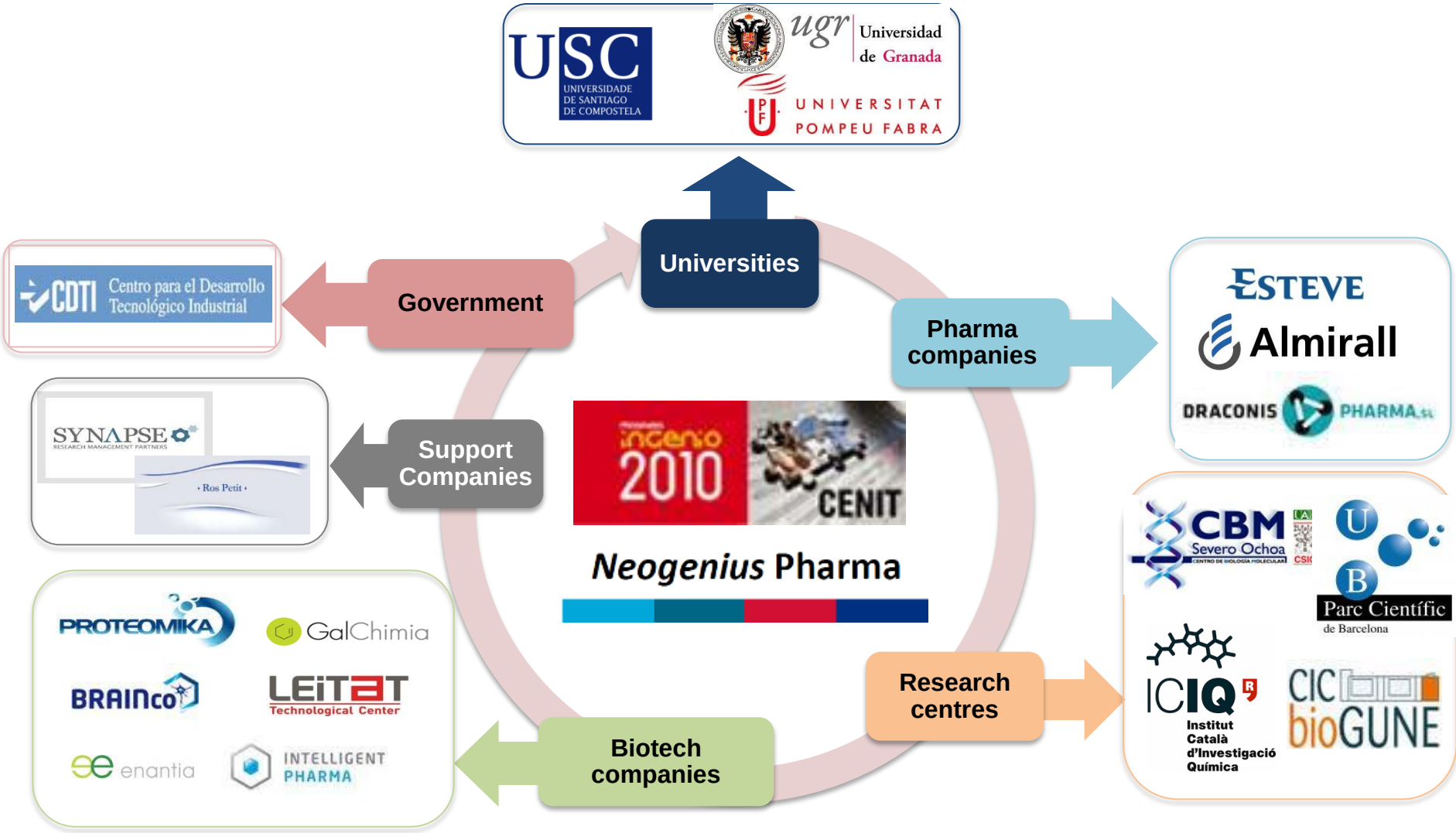
FIPCo

FIPNet

HOLNet

CENIT NEOGENIUS PHARMA

Neogenius Pharma



NEOGENIUS PHARMA: AIM

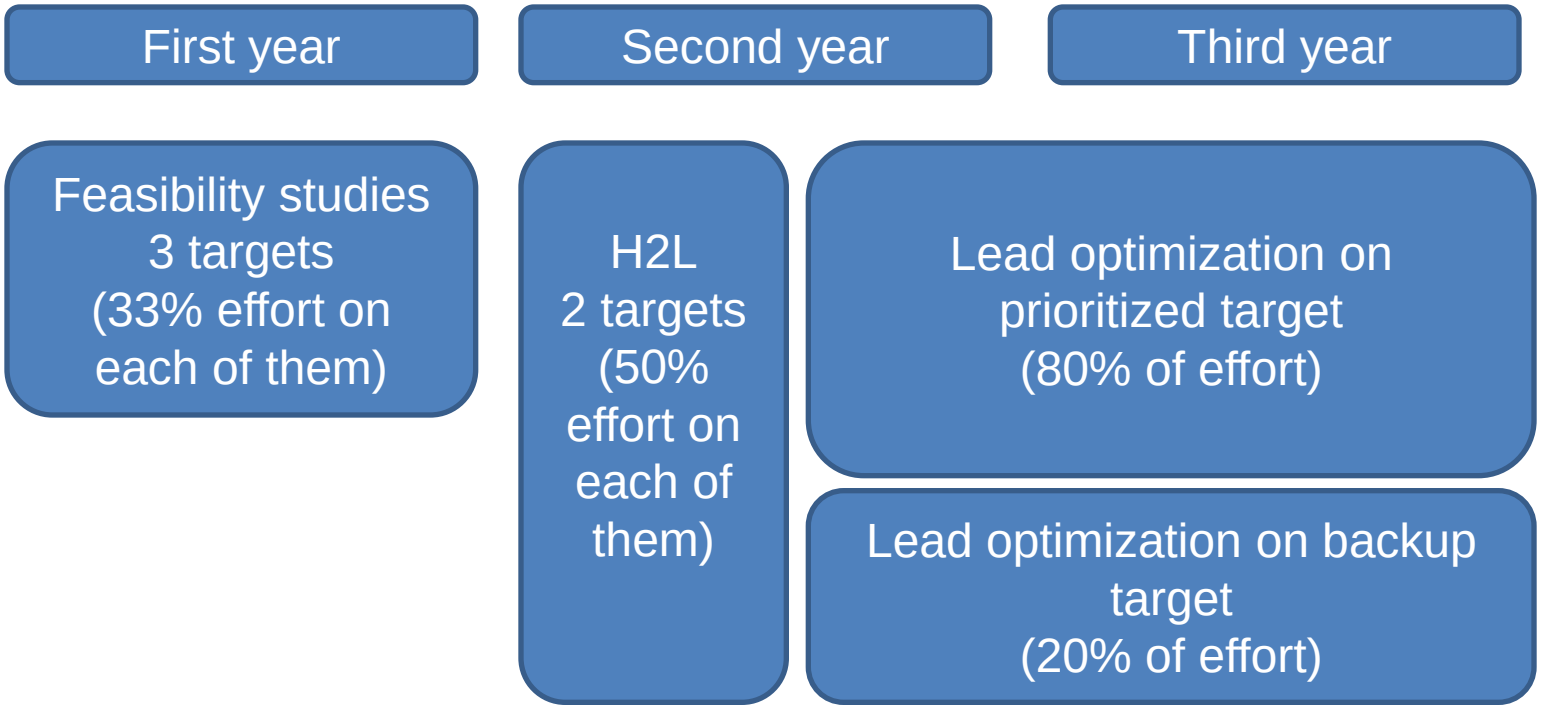
Neogenius Pharma

- Carry out a joint drug discovery program in the field of pain
  - To select a development candidate at the end of the project based on a specific Target Product Profile
  - To identify specific biomarkers for selected disease

NEOGENIUS PHARMA: APPROACH

Neogenius Pharma

- Three different targets with preclinical validation.
- Highly innovative project



NEOGENIUS PHARMA: USEF ROLE

Neogenius Pharma

Compound logistics

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USEF

In vitro screening

- Assay development
- Primary screening
- Secondary screening
- Selectivity screening

CISBIO HTRF AS PRIMARY SCREENING

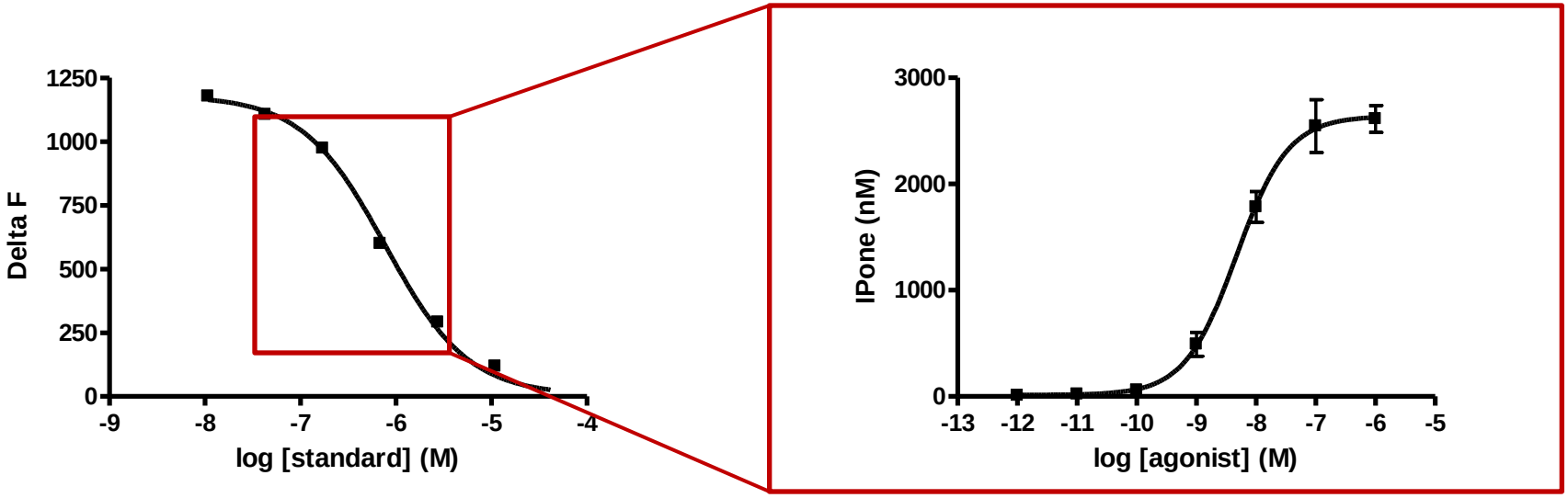
HTRF-based screening

Assay development

- HTS of the pharma companies was carried out by HTRF
- Each company developed one assay for one of the targets and then transferred the assay to the other partners.
- Assays were transferred to USEF and adapted for primary screening throughout the project

HTRF-based screening

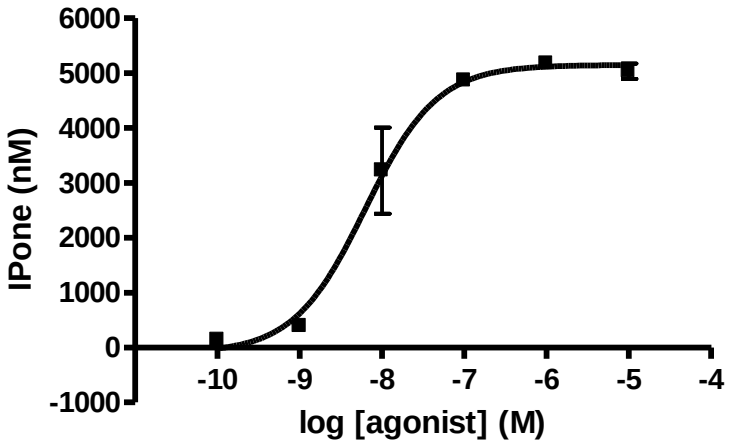
Neogenius Pharma

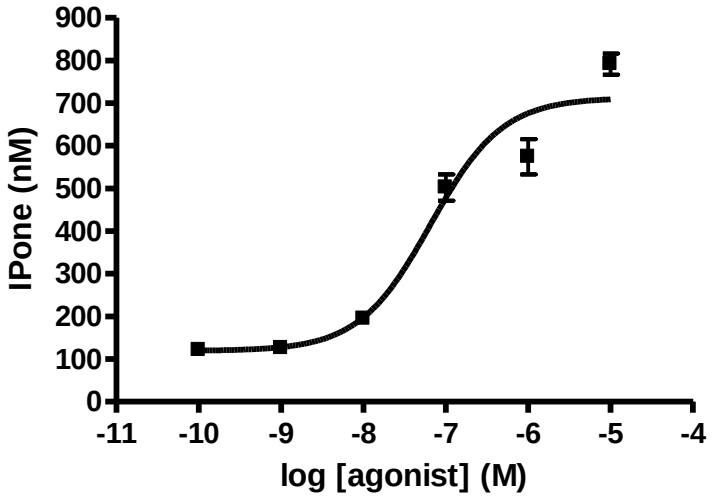


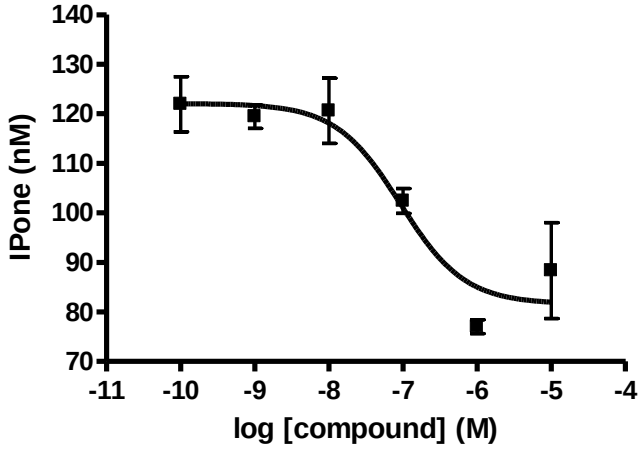
Assays were optimized for being into the appropriate range of the calibration curve

HTRF-based screening

Neogenius Pharma







Assays allowed to detect full/partial agonists, neutral antagonists and inverse agonists

HTRF-based screening

Neogenius Pharma

Target 1-Target 2

Primary screening (HTRF)

% of inhibition of agonist effect at 1 and 10 µM
(all compounds synthetized into the Target 1 and Target 2 subprojects)

% 1 µM > 50%

IC50

IC50 < 1µM

Secondary screening (binding)

Ki at either Target 1 or Target 2

Selectivity screening (binding)

% inhibition at 10 µM

Target 3

Primary screening (HTRF)

% of inhibition of agonist effect at 1 and 10 µM
(only compounds synthetized into Target 3 subproject)

% 1 µM > 50%

IC50

IC50 < 1µM

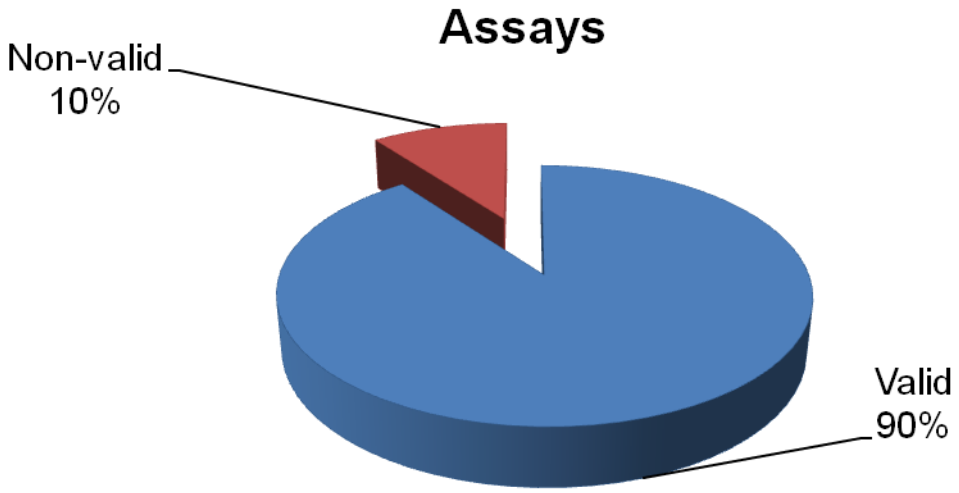
Cell-based assays

Primary screening

Neogenius Pharma

By using HTRF methodologies we have evaluated more than 2400 compounds in more than 11000 different experiments.

Assay validity was evaluated by means of different parameters: signal/background ratio, activity of reference compound, Z' score.



Compounds identified

Neogenius Pharma

Within the project we have identified compounds acting at each of the targets which were employed as tools for elucidating the role of each of the targets in pain treatment.

These compounds were used for validating one of them as a new target for pain treatment.

We have obtained several leads (in the nM range) on the validated target.

Conclusions

Neogenius Pharma

- Neogenius Pharma was the first open innovation example in drug discovery in Spain.
- This public-private consortium was able to obtain several leads at one validated target
- HTRF methodology demonstrated to be an easy to transfer methodology among 4 different labs.
- HTRF methodology was robust enough (90% of assays matching the quality controls) for being used either at HTS campaigns or as primary screening methodology.

Thanks to…

Neogenius Pharma

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… and many more from the different partners…