Integration of FDSS7000 into a modular robotic system for Open Innovation drug discovery

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Is the pharmaceutical industry open for innovation?

Pharmacogenomics Platform

An initiative from Galicia for early drug discovery
WHO WE ARE

Pharmacogenomic Platform Devoted to Knowledge valorisation

Experience

• Reference groups with over 15 years experience in genomic medicine and drug discovery. Located at the Research Centre on Molecular Medicine and Chronic Diseases (CIMUS) of the University of Santiago de Compostela (USC).

• Managing a multidisciplinary team of 130 professionals.

• Consolidated knowledge-based platform

Collaborations

• Over 30 Spanish and international pharmaceutical and biotechnology companies.

• International research groups and scientific networks at the highest level.

• Connected with the best experts in the world on strategic issues.

Validated model

• Our fundraising average is 2.5 million €/year.

• We have a self-funded and validated business model
OUR VISION

The industry is more receptive than ever to incorporate external R&D projects.

OUR CONTRIBUTION

- Validated and running knowledge-based research platform.
- Networking with the world’s best in strategic areas.

THE OPPORTUNITY

ADD talent and resources in strategic areas
- Health and social needs
- Business opportunities.

THE SOLUTION

TO OBTAIN innovative medicines
- Accelerate and increase project success.
- New model of private management innovative and cost effective.

OUR GOAL
INNOPHARMA


WHAT DOES IT AFFORDS: Technological support for boosting the Galician pharmaceutical sector by transferring the public know-how to early drug discovery projects.

Filling the gap about new targets between academic knowledge and early drug discovery programs
Open innovation and internationalization applied to a pipeline of new drug discovery programs.

Add value to programs devoted to early drug discovery to bridge the gap between basic research in new therapeutic mechanisms and its industrial application.

Provide know how and technological support infrastructure to boost the creation of new knowledge-based companies.
### INNOPHARMA: Mission

<table>
<thead>
<tr>
<th>European reference platform in early drug discovery</th>
<th>Privileged chemical library</th>
<th>Programs pipeline</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Knowledge-based technological platform already validated.</td>
<td>• Chemical and biological diversity.</td>
<td>• 110 expressions of interest.</td>
</tr>
<tr>
<td>• New translational models for in vitro efficacy and safety testing.</td>
<td>• Drugs for repurposing.</td>
<td>• International expert panel selection.</td>
</tr>
<tr>
<td><strong>Panel of innovative assays</strong></td>
<td>• Exclusive compounds.</td>
<td>• 10 collaborative projects selected from public/private entities.</td>
</tr>
<tr>
<td></td>
<td>• Biologically annotated.</td>
<td>Innovative models of knowledge and IP sharing</td>
</tr>
<tr>
<td></td>
<td>• Focused chemical libraries.</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>60000 lead-like compounds</strong></td>
<td></td>
</tr>
</tbody>
</table>
PHARMACOGENOMICS PLATFORM

- IDENTIFICATION OF NOVEL THERAPEUTIC TARGETS
  - High-throughput genotyping platforms (CEGEN)
  - Next Generation Sequencing platforms
  - Assistance for project design
  - Bioinformatics and biostatistics capabilities

- ASSAY DEVELOPMENT AND MINIATURIZATION

- IDENTIFICATION OF HITS, LEADS AND CANDIDATES
  - Screening of chemical libraries in a target
  - Hit selectivity on various targets / antitargets
  - Functional characterization of compounds in human and animal receptors
  - Lead profiling package (more than 50 studies on different targets / antitargets)
  - ADME-TOX package: cytotoxicity, safety and pharmacokinetics

Target identification & validation | Screening and hit identification | Lead identification & optimization | Candidates identification | Preclinical development | Clinical phases
---|---|---|---|---|---
Phase I | Phase II | Phase III
Post-regulatory activities
IDENTIFICATION OF PHARMACOGENOMIC BIOMARKERS FOR DRUG RESPONSE: (EFFICIENCY AND ADRS)

- Association studies (candidate gene approaches and GWAS)
- Expression analysis and functional assays
- Pharmacokinetics and pharmacodynamics correlations

PRE-DESIGNED AND CUSTOM PANELS OF ADME GENES TO PREDICT DRUG ACTIVITY ALONG THE WHOLE DRUG DEVELOPMENT PIPELINE

Drug absorption and disposition genes involved in pharmacokinetic profile (e.g. impact of genetic variation on drug action and metabolism reflected in dosing)
**Open-lab** projects
- initial stage of development
- initiative related to European networks
- open innovation

**Hit-to-candidate** projects
- fit into INNOPHARMA capabilities

**Preclinical stage** projects
- advanced stage of development
BioFarma

Company 1
In vivo Pharmacology (efficacy and safety)
Bioanalysis and DMPK
Toxicology
IP and Regulatory
(in kind)

Company 2
Medicinal Chemistry
Analytical Chemistry
Molecular Modeling
(50% in kind, 50% subcontracted)

Innopharma
Compound management
In vitro screening and assay development
Early ADME
(in kind)

External Funding

Out-licensing

Hit Finding
Hit to Lead
Lead Optimization
Preclinical Development
Phase I
Phase II (PoC+ IIb)
Phase III
Submission to Launch
Launch

<table>
<thead>
<tr>
<th>Time (years)</th>
<th>0.75</th>
<th>0.75</th>
<th>1.50</th>
<th>0.90</th>
<th>1.30</th>
<th>1.80</th>
<th>2.20</th>
<th>1.30</th>
<th>10.50</th>
</tr>
</thead>
<tbody>
<tr>
<td>pTS</td>
<td>0.80</td>
<td>0.75</td>
<td>0.85</td>
<td>0.70</td>
<td>0.70</td>
<td>0.60</td>
<td>0.80</td>
<td>0.90</td>
<td>0.11</td>
</tr>
<tr>
<td>Cost per Phase (M€)</td>
<td>0.80</td>
<td>1.50</td>
<td>5.00</td>
<td>1.50</td>
<td>1.60</td>
<td>15.00</td>
<td>80.00</td>
<td>20.00</td>
<td>125.40</td>
</tr>
</tbody>
</table>

3 years
3 years
Measurement of **GPCR** activity by intracellular Ca$^{2+}$ quantification (Calcium-4)
AUTOMATED ASSAY DEVELOPMENT

Agonist mode

Ex480:En540 with SB

Antagonist mode

Ex480:En540 with SB
QUALITY CONTROL

![Graph showing data points for Plate #1 to #7 with corresponding Z values.]
### AGONIST MODE: RESULTS

<table>
<thead>
<tr>
<th>Compound</th>
<th>EC\textsubscript{50} (nM)</th>
<th>E\textsubscript{max} (% E\textsubscript{max} endogenous agonist)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Agonist 1</td>
<td>5.3</td>
<td>100</td>
</tr>
<tr>
<td>Agonist 2</td>
<td>26.6</td>
<td>100</td>
</tr>
<tr>
<td>Agonist 3</td>
<td>9.1</td>
<td>70</td>
</tr>
<tr>
<td>Agonist 4</td>
<td>7.2</td>
<td>71</td>
</tr>
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</table>
### Antagonist Mode: Results

<table>
<thead>
<tr>
<th>Compound</th>
<th>IC&lt;sub&gt;50&lt;/sub&gt; (nM)</th>
<th>K&lt;sub&gt;B&lt;/sub&gt; (nM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antagonist 1</td>
<td>195.2</td>
<td>65.1</td>
</tr>
<tr>
<td>Antagonist 2</td>
<td>162.0</td>
<td>54</td>
</tr>
</tbody>
</table>
SUMMARY

• INNOPHARMA is an academic initiative for adding value to basic research projects in early drug discovery in an Open Innovation framework.

• It is based on three pillars: Chemical library, open innovation projects and innovative assays.

• GPCR primary screens will be run in an automated platform and read using FDSS7000 (Ca2+, aequorin, etc.).

• Calcium-based assays have been developed looking for either agonists or antagonists in the same experiment.

• Assays showed to be robust and allowed to identify reference compounds distributed in 7 384-well plates.