Programa Cooperación Farma-Biotech
Jornada IV: Ámbitos terapéuticos relacionados con respiratorio, dermatología, nefrología, inflamación e infección

**UR-63325 for the treatment of asthma and rhinitis**

**UR-67767 for the treatment of inflammatory diseases**

Madrid, 12 July 2011
Content

1. Palau Pharma: brief overview

2. The Products: UR-63325 and UR-67767
   a) Therapeutic focus
   b) Innovative mechanisms of action
   c) Differential features facing the market
   d) Current status of development
   e) IPR protection
   f) Pitfalls & Risks to be considered

3. Availability for cooperation
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A Company Founded On Solid Market Needs

- Biopharmaceutical company based in Barcelona, Spain
- Created through a spin-out from Grupo Uriach in 2006
- Focused on the discovery and development of new small molecule drugs for the treatment of inflammatory and autoimmune diseases
- Innovative pipeline consisting of 6 clinical stage development compounds
- Validated business model through several successful partnerships
- €40 M raised on inception
- Shareholders:

[Brand Logos and Senior Management Section]
A Strategy Designed For Solid Results

• Build early positive differentiation from competitors’ molecules
• Create value by developing projects to human Proof-of-Concept
• Use a dual approach to balance the risk profile
  - Drug discovery platform as a source of new projects
  - In-license programs to grow and diversify the portfolio
• Partner for late-stage development and commercialization
A Strategy Designed For Solid Results

> **Our Approach**
  - Small molecules
  - Oral route
  - Preclinical or clinical validated targets

> **Main fields of interest**
  - **Respiratory**: allergic rhinitis, asthma, COPD
  - **Skin**: atopic dermatitis, psoriasis
  - **Neurological**: neuropathic pain
  - **Autoimmune**: rheumatoid arthritis, IBD, lupus
### Turning Unmet Needs Into Solid Drugs

<table>
<thead>
<tr>
<th>Project</th>
<th>Indication</th>
<th>Discovery</th>
<th>Preclin.</th>
<th>Phase I</th>
<th>Phase II</th>
<th>Phase III</th>
<th>Market</th>
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<tbody>
<tr>
<td><strong>ACTIVE® and IRIST® STENTS</strong></td>
<td>Coronary</td>
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<td></td>
<td>Restenosis</td>
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<td>Vétoquinol</td>
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<td><strong>CIMALGEX®</strong></td>
<td>Inflammatory diseases, pain (veterinary product)</td>
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<td><strong>Albacaonazole</strong></td>
<td>Fungal infections</td>
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<td><strong>Cimicofib</strong></td>
<td>Depression</td>
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<td><strong>Deralazine sodium</strong></td>
<td>Ulcerative colitis</td>
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<td><strong>UR-13870 (p38 MAPK Inhibitor)</strong></td>
<td>Neuropathic pain, rheumatoid arthritis</td>
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<td><strong>UR-63325 (H₄R antagonist)</strong></td>
<td>Asthma, allergic rhinitis</td>
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<td><strong>UR-65318 (H₄R antagonist)</strong></td>
<td>Atopic dermatitis</td>
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<td><strong>UR-67767 (Jak inhibitor)</strong></td>
<td>Inflammatory, autoimmune diseases</td>
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<td><strong>Neogenius Pharma (new target)</strong></td>
<td>Inflammatory diseases</td>
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<td><strong>Dendria (new target)</strong></td>
<td>Neuroinflammatory diseases</td>
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Histamine: “well-known” mediator acting through four receptors - H1, H2, H3 and H4

**H1 in SMC and EC**

**H2 in Parietal Cells**

**H1 and H3 in CNS**

**H4: Inflammatory cells**

- **H4R**, also a GPCR
- Mainly expressed in inflammatory and immune cells (eosinophils, mast cells, dendritic cells, lymphocytes, etc)
- Very high affinity for histamine
- Implicated in chemotaxis and cytokine production

**UR-63325 for Asthma and Allergic Rhinitis**

- Novel mechanism of action: Selective Histamine H₄ receptor antagonist (H₄R)
- H₄R highly expressed in bone marrow and white blood cells
- Oral treatment
- Anti-inflammatory activity
- Safe and very well tolerated in healthy volunteers
- Patent protected in all main relevant markets with potential maximum expiry dates of 2033

**Unmet medical needs**

- New mechanisms with improved efficacy
- Alternatives to steroids for disease control
- Impact on co-morbidities such as asthma in allergic rhinitis patients
- Improve patient compliance
Preclinical data

- **Very active and selective** $H_4R$ antagonist
- **Good activity** in several rodent models of asthma
  - improves respiratory function parameters
  - inhibits pulmonary inflammation
- **Good ADME and PK** profile
- **Clean safety and toxicology** profile
- Safety margins allow the compound to enter into first-in-man clinical trial
UR-63325 for Asthma and Allergic Rhinitis

Clinical data

- SAD and MAD studies complete
- Very good PK linearity
- Half life supports once daily administration
- Excellent safety
- Dose dependent, potent and sustained inhibition of an H₄R-related biomarker
- PIb/IIa study started in Dec 2010. Interim results are due in Q3 2011
UR-67767 for Inflammatory and Autoimmune diseases

- A potent balanced Jak inhibitor (Jak1, Jak2, Jak3 and Tyk2)
- Inflammatory and autoimmune diseases
- Next generation of small molecules with the potential to be as potent as biological treatments
- Preclinical testing

- UR-67767 is a potent balanced Jak (including Tyk2) specific inhibitor with a very competitive efficacy and safety profile over compounds ahead in development
- Excellent efficacy in models of autoimmune disease such as rheumatoid arthritis, multiple sclerosis, psoriasis
- Very good safety profile up to 14 days repeated doses in three different animal species
- Patent protected in all main relevant markets with potential maximum expiry dates of 2035

Unmet medical needs

- New targets widening scope of current biological therapies may increase efficacy/safety
- Long term treatments with appropriate safety (avoiding concerns on long term malignancy and infections)
- Oral therapies with efficacy comparable to those of biological agents
**UR-67767 for Inflammatory and Autoimmune diseases**

**Preclinical data**

- **Balanced and potent** inhibitor of the four Jak isoenzymes
- **Good activity** in several rodent models of inflammation
  - Rheumatoid Arthritis (CIA and AIA) UR-67767 displays outstanding oral efficacies, both reducing the inflammation, the cartilage damage and bone erosion
  - Multiple sclerosis (MOG-EAE in mice). UR-67767 shows a high activity in both prophylactic and therapeutic treatments
  - Psoriasis (ex-vivo model in human psoriatic explants). UR-67767 inhibits the expression of genes that play key roles in psoriasis.
- **Excellent ADME** profile
- **Good safety and toxicology** profile
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Palau’s final goal is to create differentiated and revolutionary new medicines that target the unmet needs of patients that suffer from inflammatory and autoimmune diseases.

To give the right solution to patients, Palau does not work alone.

Partnering plays a strong role in both Palau’s business model and its development philosophy.

Palau strongly believes that:

- establishing alliances is a good option to move the science forward in a faster and more productive way.
- the key to success is forming complementary partnerships defined by commitment, close collaboration and transparent communication.

Therefore, Palau is open to discuss different and creative ways of cooperation.