

## > PROJECT FACTSHEET: UR-65318

***There is a strong need for novel and innovative approaches to treat atopic dermatitis that control the early symptoms, such as itch, and keep sustained remission, while maintaining both efficacy and a very good safety profile.***

***UR-65318 is intended to cover such requirements by providing anti-inflammatory activity and efficacy in atopic dermatitis symptoms, including pruritus. The potential allowance for chronic administration, due to its excellent safety profile, will compete favourably with current therapy.***

### > A Company Founded On Solid Market And Patients Needs

Palau Pharma, S.A. ("Palau") is a product-driven biopharmaceutical company focused on the discovery and development of revolutionary and differentiated new medicines that are designed to address the unmet needs of patients suffering from inflammatory and autoimmune diseases. Our core business model is to develop novel drugs through Phase IIa clinical trials. At that point, we decide whether to keep the development in-house or partner the compound for further development and commercialization. We have a broad portfolio of projects at different stages of development from early discovery to the late clinical stages, and have forged partnerships with leading pharmaceutical companies such as GlaxoSmithKline.

Our R&D strategy is focused on developing "best-in-class" or "first-in-class" drugs that modulate the activity of validated targets with established preclinical or clinical proof-of-concept. Based on a unique and high-quality cost-effective structure, our final objective is to achieve early positive differentiation from our competitor's molecules by addressing their limitations and designing a clear, focused and fast path to commercial success.

### > The Target: Histamine H<sub>4</sub> Receptor

The histamine H<sub>4</sub> receptor (H<sub>4</sub>R) is a G-protein coupled receptor that is widely distributed in skin and is over expressed in atopic dermatitis patients. Data from several preclinical *in vitro* and *in vivo* studies suggest that this novel target plays a key role in allergic and immuno-inflammatory disorders. Furthermore, the H<sub>4</sub>R regulates chemotaxis of inflammatory cells and has been proven to be highly involved in the mechanism of pruritus.

### > The Opportunity: A New Treatment for Atopic Dermatitis

UR-65318 is the first H<sub>4</sub>R antagonist for the treatment of atopic dermatitis. The compound has been recently selected for ICH preclinical development.

The mechanism of action of UR-65318, together with its drug profile, forecast that its use may positively affect some of the most important unmet needs in atopic dermatitis, including controlling itch, the most relevant need for this indication.

### > Solid Results

UR-65318 has been chosen as the candidate for development, after testing more than 3000 molecules in our *in vitro* and *in vivo* drug discovery assays.

*In vitro* tests included binding affinity and off-target selectivity, H<sub>4</sub>R-dependent functional assay, cytotoxicity and *in vitro* metabolism. In the confirmation phase, our molecules have been tested in several well established atopic dermatitis models.

UR-65318 displays high affinity and selectivity for the H<sub>4</sub>R. The proof-of-principle for the use of an H<sub>4</sub>R antagonist in the treatment of atopic dermatitis has been confirmed with consistent results obtained in different animal models. In one of these models, gene expression study has shown that the candidate is able to inhibit the overexpression of inflammatory molecules.

#### At a glance

- Founded: November 2006
- Spin-out from Grupo Uriach
- Employees: 85
- €40M raised at inception

#### Management

- **Ignacio Faus**  
Chief Executive Officer
- **Manel Barallat**  
Chief Financial Officer
- **Xavi Bartrolí**  
Director of Innovation & Drug Discovery
- **Manuel Merlos**  
Director of Drug Development & Clinical Research
- **Heidi Sisniega**  
Head of Business Development & Licensing
- **Neus Virgili**  
Head of Patents & Legal Affairs
- **Caridad Pontes**  
Head of Clinical Research & Regulatory Affairs

#### Shareholders

- Grupo Uriach
- Caixa Catalunya
- Caja Duero
- Andosins Capital
- Najeti Capital
- Senior Management

#### Scientific Advisory Board

- Dr. Roderick Flower
- Dr. Desmond Fitzgerald
- Dr. Alberto Grignolo
- Dr. Trevor Hansel
- Dr. Thomas Luger



In the NC/Nga atopic dermatitis mouse model, the administration of UR-65318 improves parameters such as the skin epithelial structure (Fig.1) and pruritus and shows comparable efficacy to gold standard Protopic™ (Fig. 2). This outcome represents a compelling preclinical validation of our H<sub>4</sub>R candidate in atopic dermatitis. Toxicology and safety data obtained so far forecast a very broad safety margin.

The development plan has been established, and preclinical regulatory studies are due to start in Q3 2010.

#### UR-65318

- New Mechanism of action: Histamine H<sub>4</sub> receptor antagonist
- First in class
- High affinity and selectivity
- Very active in several animal atopic dermatitis models
- Development stage: Preclinical

#### Restoration of epithelial structure (NC/Nga mice model)

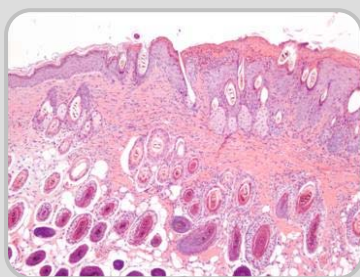
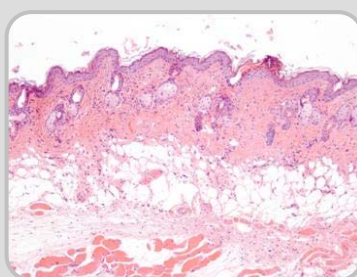


Fig. 1

Control



H<sub>4</sub>R antagonist

#### Clinical Score (NC/Nga mice model)

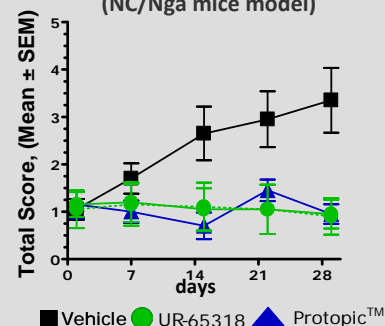


Fig. 2

#### > Intellectual Property

Palau's research in the H<sub>4</sub>R field has resulted in the filing of ten patents, seven of which are published.

#### > Every Partnership Is a Solid Commitment

Palau is seeking to establish a creative and value-driven strategic alliance with a leading biopharmaceutical company for the late stage development and commercialization of UR-65318.

#### Contacts

For further information on Palau Pharma and its products, please visit

[www.palaupharma.com](http://www.palaupharma.com)

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