

> PROJECT FACTSHEET: UR-63325

Current asthma therapies are mainly inhaled treatments providing only local effects with an inconvenient type of delivery. Oral treatments targeting the entire respiratory tract, such as montelukast, present a limited efficacy.

UR-63325 is an orally administered and highly safe agent that might influence the allergic process and avoid airway inflammation in both the nose and the bronchi. This new approach may provide a substantially improved treatment to patients with coexistence of asthma and rhinitis, and would definitively provide broader therapeutic options in this field.

> 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 H₄ Receptor

The histamine H₄ receptor (H₄R) is a G-protein coupled receptor highly expressed in bone marrow and white blood cells. Its distribution and data from several *preclinical in vitro* and *in vivo* proof-of-principle studies strongly suggest that this novel target plays a key role in allergic and immuno-inflammatory disorders.

> The Opportunity: A New Oral Treatment for Allergic Asthma and Rhinitis

New promising therapies for respiratory inflammatory diseases will be those able to control inflammation, increasing compliance and reducing or avoiding corticosteroids side effects.

Palau's UR-63325 is the first reported H₄R antagonist for the oral treatment of allergic respiratory disorders entering clinical development. UR-63325 has finished a Phase I single dose clinical trial with favorable safety data and an excellent pharmacokinetic profile. The compound is currently in Phase I multiple dose clinical trial.

> Solid Results

UR-63325 has an excellent preclinical profile. It displays good affinity and selectivity on the H₄R. *In vivo*, Palau's H₄R antagonist has shown good anti-inflammatory activity in mouse and rat asthma models by reducing allergen-induced bronchial hyperreactivity and lung inflammatory markers to an extent similar to that observed with dexamethasone. Moreover, UR-63325 has shown significantly better results than the comparator montelukast in a rat OVA-induced asthma model. The favorable pharmacodynamic (PD) and pharmacokinetic (PK) data, together with a comprehensive toxicology and safety package has allowed the progression of UR-63325 into clinical development.

The regulatory preclinical package to support clinical trials up to 28 days treatment was successfully completed.

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 Bartolí**
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



The program has successfully completed the Phase I single ascending dose First-in-Man clinical trial. Eight cohorts were treated from 2 mg to 100 mg of UR-63325 (6 treated / 2 placebos per cohort). UR-63325 has proven to be safe and well tolerated showing very good PK and PD results. Good safety results are consistent with the excellent profile demonstrated in preclinical studies, and predicted PK values from animal species fit with actual human data. The compound shows PK linearity and the long half-life fully supports a once daily administration (Fig.1). The biological activity of UR-63325 in this clinical trial was proven measuring an H4R-related biomarker and the results obtained suggest sustained activity (Fig.2).

UR-63325

- New Mechanism of action: Histamine H₄ receptor antagonist
- First-in-class
- High affinity and selectivity
- Very active in several animal asthma models
- Excellent PK profile compatible with once daily administration
- Development stage: Phase Ib/IIa

Plasma UR-63325 concentrations-time profile after administration of single rising oral doses

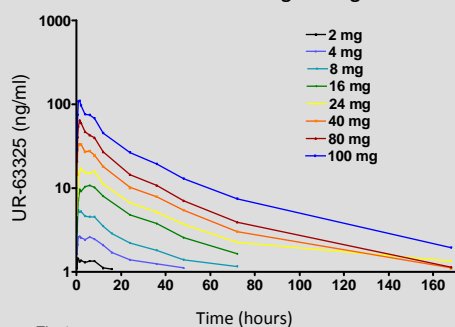


Fig.1

Biomarker of H₄R activity in the First-in-Man clinical trial

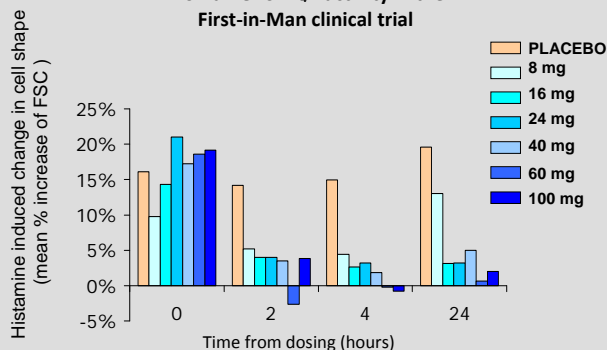


Fig.2

A Phase I multiple ascending dose clinical trial is in progress. Five different cohorts will test sequentially increasing doses of UR-63325 given once daily for seven consecutive days. Besides safety and PK parameters, biomarkers will be also measured allowing the evaluation of the biological activity and potential clinical relevance.

Results of the Phase I multiple ascending dose clinical trial are due in Q4 2010.

An efficient synthetic process has been developed and has been scaled-up to produce kg-batches. Eighteen months stability data for the API are available.

> Intellectual Property

Palau's research in the H₄R 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-63325.

Contacts

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

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