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





MEDICAMENTOS INNOVADORES Plataforma Tecnológica Española



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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









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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:



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

Project	Indication	Discovery	Preclin.	Phase I	Phase II	Phase III	Market
ACTIVE [®] and IRIST [®] STENTS	Coronary Restenosis						
CIMALGEX®	Inflammatory diseases, pain (veterinary product)						
Albaconazole	Fungal infections						
Cimicoxib	Depression						
Dersalazine sodium	Ulcerative colitis						
UR-13870 (p38 MAPK Inhibitor)	Neuropathic pain, rheumatoid arthritis						
UR-63325 (H ₄ R antagonist)	Asthma, allergic rhinitis						
UR-65318 (H ₄ R antagonist)	Atopic dermatitis						
UR-67767 (Jak inhibitor)	Inflammatory, autoimmune diseases						
Neogenius Pharma (new target)	Inflammatory diseases						
Dendria (new target)	Neuroinflammatory diseases						

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Histamine: "well-known" mediator acting through four receptors - H1, H2, H3 and H4



PLC-B

Ins(1,4,5)P, DAG

SC:n2+1 1

Ptdins(4,5)P2

- 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

RL Thurmond. Nature Reviews in Drug Discovery 2008, 7: 41-53

UR-63325 for Asthma and Allergic Rhinitis

- Novel Oral treatment: First-in-class compound
- Allergic respiratory diseases: asthma and allergic rhinitis
- Alternative to oral anti-leukotrienes and inhaled treatments with limited efficacy or that provide only local effects
- Phase Ib/IIa clinical trials ongoing
- 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

UR-63325 for Asthma and Allergic Rhinitis

Preclinical data

- Very active and selective H₄R 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 H₄Rrelated 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